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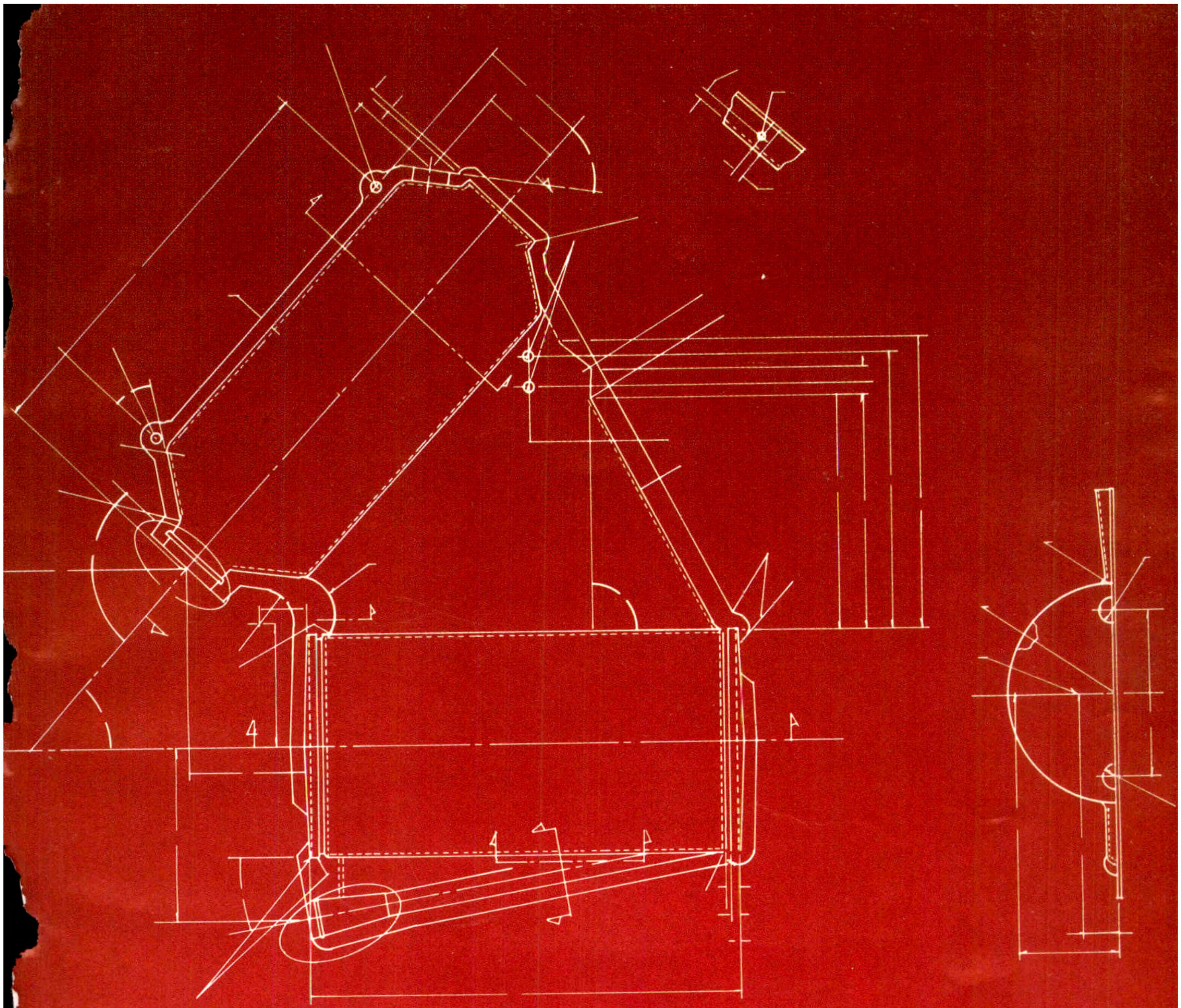

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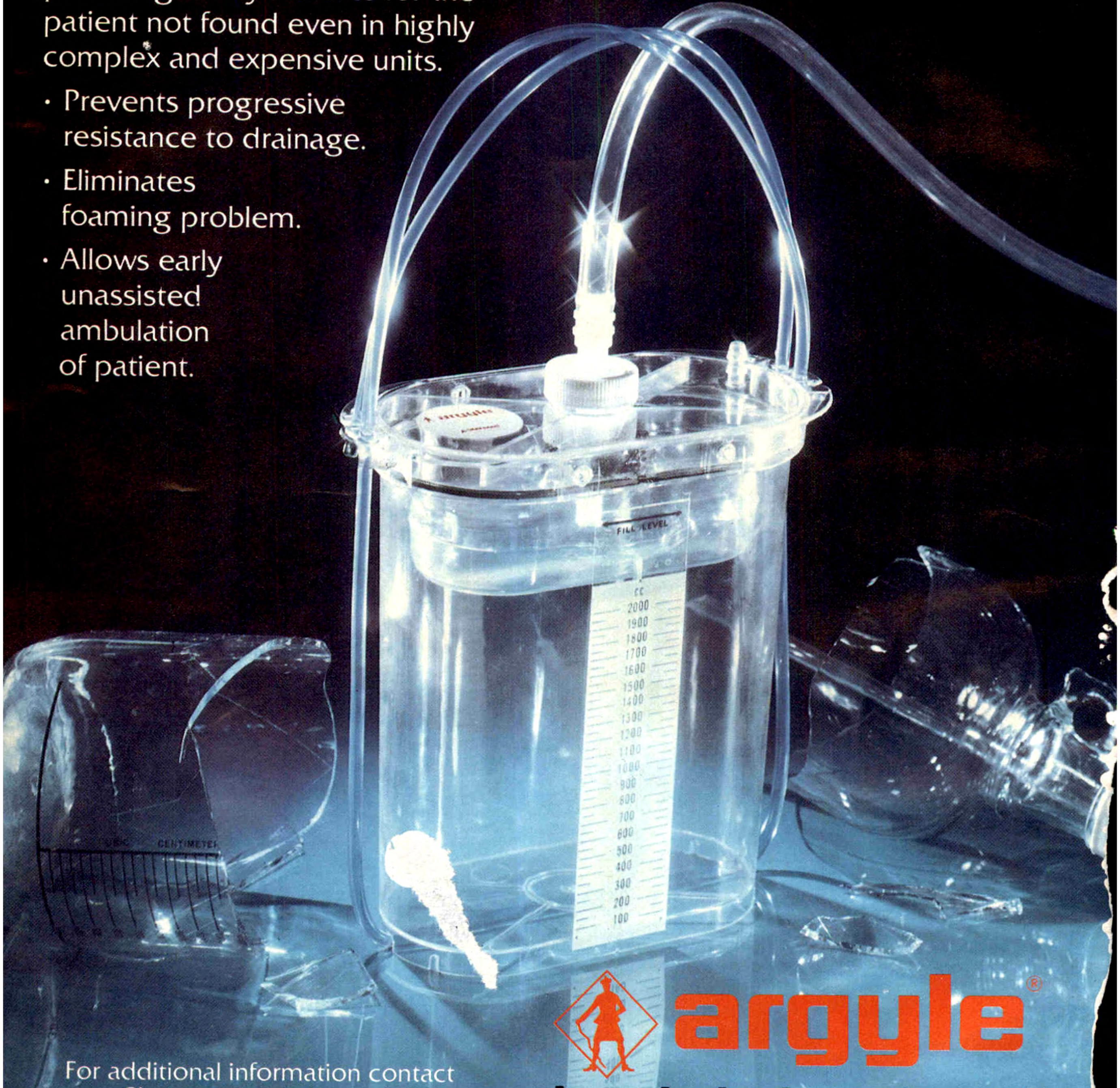

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Volume 22 Number 2 August 1976

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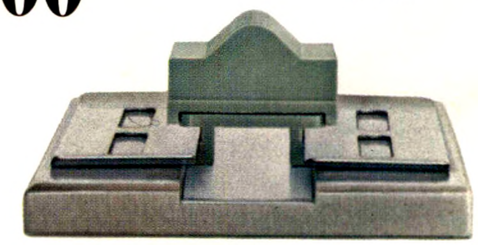

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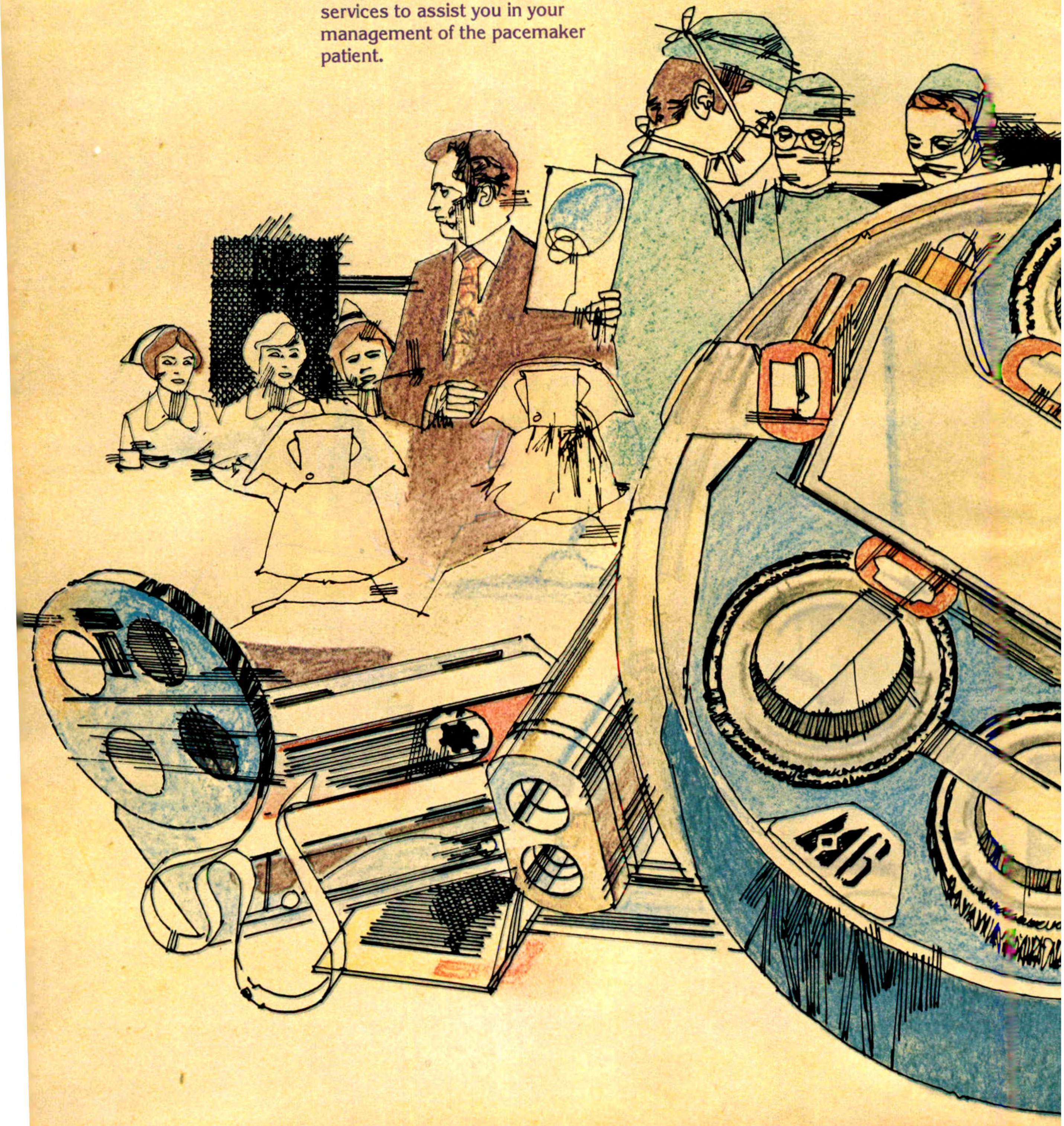

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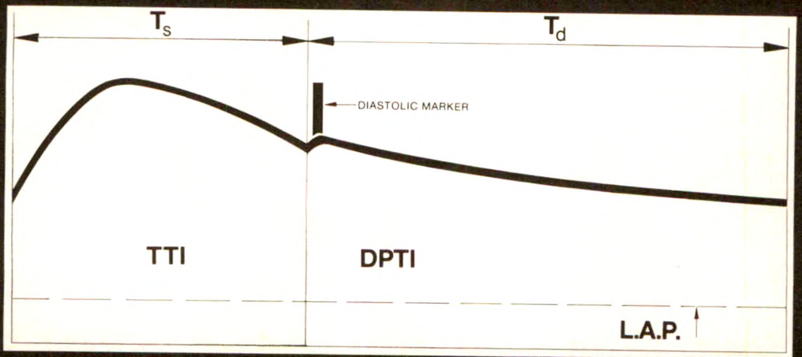

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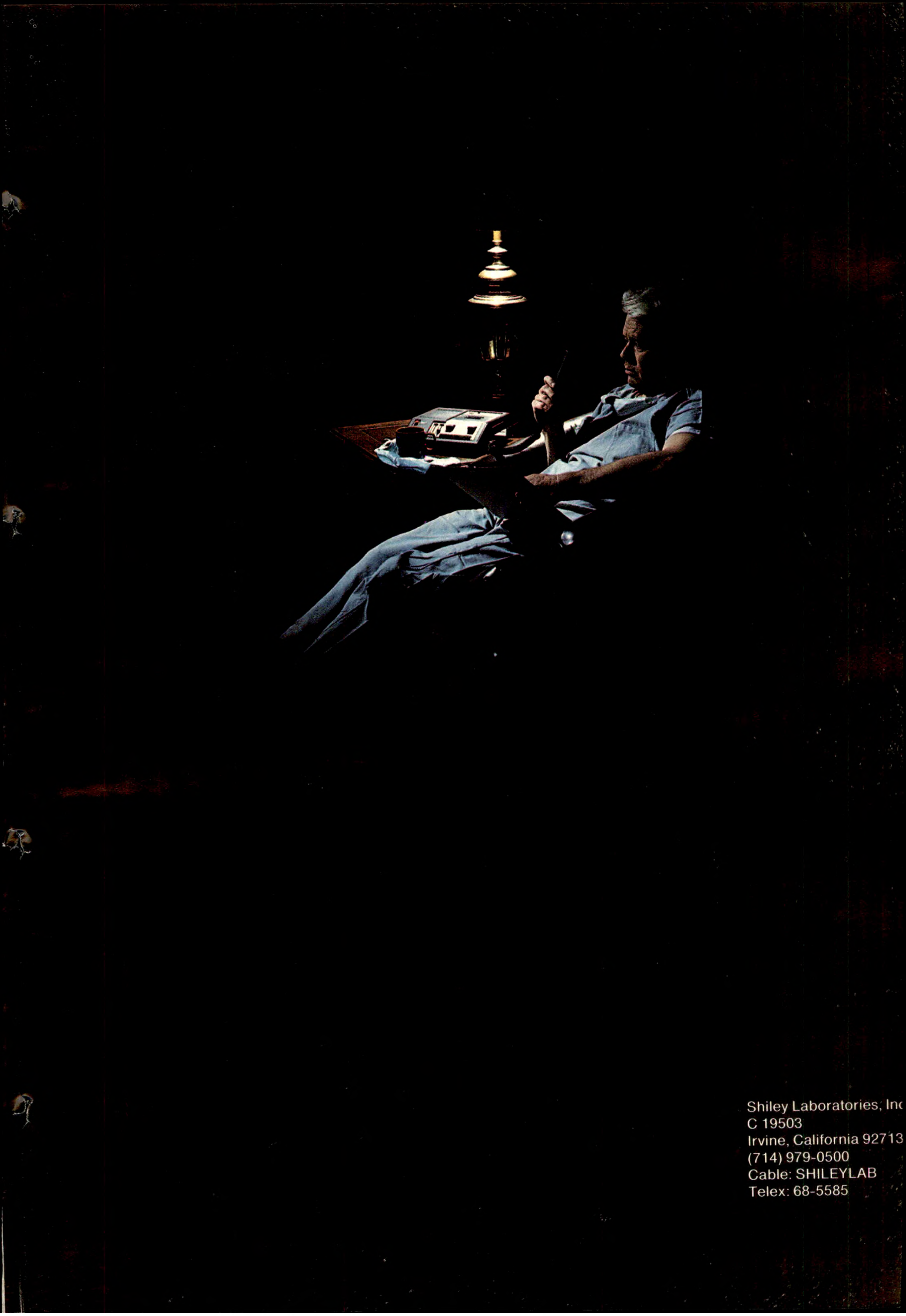

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THE ANNALS OF THORACIC SURGERY Vol 22 No 2 August 1976

Permanent Extracorporeal Esophagogastric Tube for Esophageal Replacement

David B. Skinner, M.D., and Tom R. DeMeester, M.D.

ABSTRACT **Six patients are presented in whom an extracorporeal esophagogastric tube bypass was employed in lieu of standard methods of esophageal reconstruction. These tubes, obtained from Japan, have functioned well in 4 of the 6 patients. This approach offers an alternative to gastrostomy feedings alone in a patient with advanced esophageal disease in whom no other method of surgical reconstruction can be offered.**

Occasionally, patients having advanced esophageal disease are unsuitable candidates for standard techniques of esophageal reconstruction. Permanent gastrostomy and cervical esophagostomy may be necessary. In 1969, Ikeda and Fukishima of Yokohama, Japan, informed us of the extracorporeal esophagogastric tubes developed by Akiyama. In Japan these tubes sometimes are used in lieu of reconstruction following esophagectomy for carcinoma [1, 2]. Such tubes, obtained from Japan, have been used in 6 patients. We have not found a description of this method in an English language report.

The available set of tubes* includes a gastrostomy tube, two esophagostomy tubes, a plastic connector, and a clamp (Fig 1). The tubes are made of silicone-coated rubber. The gastric tube has a 60-degree angle at the neck and ends in a large, mushroom-shaped flange. The esophageal tubes have a 45-degree bend at the neck. One of them has a small mushroom-shaped flange and is used during the initial stages of application. The second esophageal tube has a larger mushroom, to be used after a subcutaneous pocket is developed in the esophageal stump. Sets of tubes come in three sizes, having internal diameters of 11, 12.5, or 14 mm.

Technique of Insertion

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The cervical esophagostomy is generally performed in the left side of the neck but may be done on the right. The cervical esophagus is exposed through an incision passing anterior to the sternocleidomastoid muscle and between the thyroid gland and trachea medially and the carotid sheath laterally. The esophagus is mobilized from its prevertebral location, taking care not to injure the recurrent laryngeal nerves. At least a 4 cm segment of esophagus below the cricopharyngeus should be employed. After the esophagus is divided, the distal end is sutured closed. The stump is brought through the incision to the level of the skin. The stoma may be placed either in the medial aspect of the skin incision or through a separate stab wound, depending on where it lies easily without tension or angulation. As the incision is closed, the muscular layers of the esophagus are anchored to the cervical fascia and to the subcutaneous tissue. The full thickness of the esophagus is anastomosed to the dermis with multiple interrupted sutures. The esophageal stoma is allowed to heal for several weeks. It is important that the stoma be dilated as necessary so that a finger can easily be passed through it. If this is not done,

From the Department of Surgery, University of Chicago Hospitals and Clinics, and the University of Chicago Pritzker School of Medicine, Chicago, IL.

Presented at the Twelfth Annual Meeting of The Society of Thoracic Surgeons, Washington, DC, Jan 26–28, 1976.

Address reprint requests to Dr. Skinner, Department of Surgery, University of Chicago Hospitals and Clinics, 950 E 59th St, Chicago, IL 60637.

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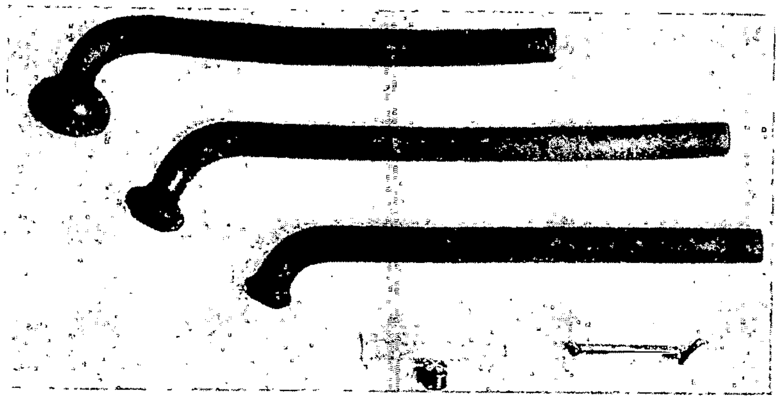


Fig 1. The tube set includes, from top to bottom, a gastrostomy tube, two esophagostomy tubes, a connector with vent, and a clamp.

the stoma contracts and makes it impossible to insert the tube.

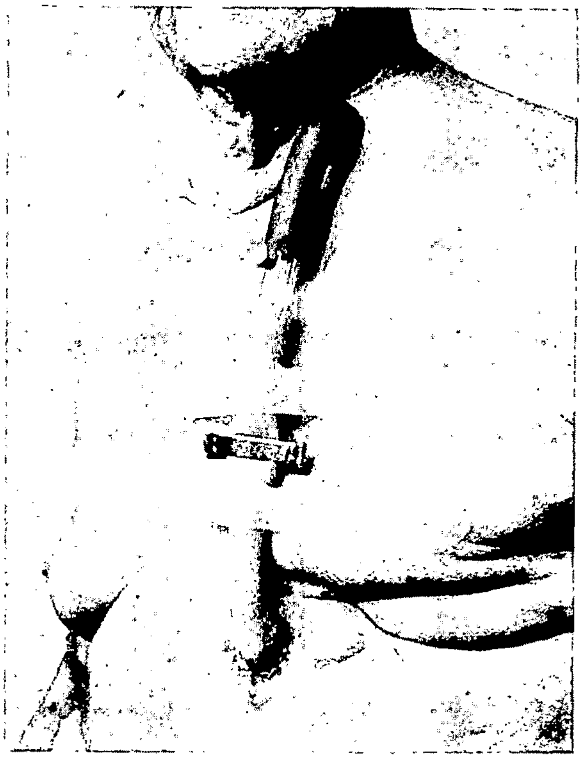
After healing is complete, the esophageal tube with the small mushroom flange is gently inserted. The mushroom is folded on itself to reduce its diameter until it lies in the esophagus beneath the skin; then the tube is allowed to snap open to fill the esophageal lumen. With the patient standing completely erect or lying supine, the esophageal tube is shortened so that it attaches by the plastic connector to the gastric tube with a slight bit of redundancy. This arc in the connected tubes keeps some pressure on the esophageal tube, which helps to maintain it in position (Fig 2).

Initially the patient is instructed to swallow liquids, and eventually he advances to a solid diet as confidence and experience are gained. Meals are eaten sitting upright to prevent free reflux and aspiration. Between meals the gastric tube is clamped and the esophageal tube is removed to prevent irritation of the skin. Patients quickly learn the technique of inserting the esophageal tube. A pediatric stomal appliance works well for collecting saliva and secretions from the cervical stoma between meals and during sleep. The esophageal tube should never be left in place overnight due to the dangers of skin breakdown and ulceration.

Technical Problems

The gastric tube functions without leaking if the mushroom flange is held against the abdominal wall. This may require placing a gauze pad under the stem of the tube to hold it forward. The gastric tube deteriorates with time and needs to be changed at three- to six-month intervals. This is generally done without hospitalization of the patient or undue difficulty. Another common problem is leakage around the esophageal tube. As the pocket for the flange in the subcutaneous tissue enlarges, it is necessary to shift to the tube with the larger mushroom flange or to a larger caliber tube. Adjusting the

Fig 2. The tubes in place in Patient 5.



angle of exit of this tube from the stoma is important in correcting leakage around the tube. Gauze pads strategically placed beneath the tube may assist in this. It is essential that the stoma be dilated daily and the tube inserted to prevent contraction. If contraction occurs, it may be necessary to perform a Z-plasty revision of the cervical stoma. If the esophageal stump is too short, peristaltic contraction will tend to pull the esophagus away from the skin and lead to formation of a cicatricial band. If the stump is markedly short, there may be insufficient length for the flange of the tube to ride below the cricopharyngeus, and the tube will not be tolerated by the patient.

Illustrative Cases

Patient 1

A 59-year-old white man was first seen in October, 1969, because of an esophageal stricture. Biopsies demonstrated adenocarcinoma arising in an esophagus lined with columnar epithelium. Subtotal esophagectomy with radical mediastinal node dissection and partial gastrectomy was performed. Mediastinal lymph nodes contained metastases. A cervical esophagostomy and gastrostomy were placed temporarily while the patient was prepared for a colon bypass.

One week after a substernal left colon interposition, it was apparent that the bowel segment had infarcted, and it was removed. Following recovery, the patient was fitted with the extracorporeal esophagogastric tubes. These were well tolerated, and the patient refused a proposed right colon or gastric interposition. For the remaining eighteen months of his life he ate a regular diet at home or in public with the tubes, experienced a 10.4 kg weight gain, and resumed his work as a business executive. He required one revision of the cervical stoma because of stenosis early in his recovery. Death was caused by extensive metastases.

Patient 2

A 64-year-old white woman underwent radical near-total esophagectomy in January, 1971, following preoperative radiation therapy for squamous carcinoma of the upper third of the esophagus. A 1 cm cuff of esophageal stump was left below the cricopharyngeus. Right colon bypass was attempted but failed because of venous infarction. After she recovered from this, the cervical and gastric stomas were prepared for insertion of the extracorporeal tubes.

The cervical stump was too short for the patient to tolerate the tube except for short periods. As a result, the palliation achieved with the tubes was poor. The patient subsisted on gastrostomy tube feedings during the remaining year of her life before dying of metastatic disease.

Patient 3

A 70-year-old white man was referred in April, 1971, when he developed a tracheoesophageal fistula during radiation therapy for squamous carcinoma of the middle third of the esophagus. The patient refused a bypass operation. Accordingly, the cardia was transected and closed, and the Japanese gastrostomy tube was inserted. The cervical esophagus was divided, the distal end was closed, and a stoma was created.

The patient received nutrition through the gastric tube initially and eventually through the esophagogastric tube connection. Because of depression due to his illness, the patient went for several days at a time without using the esophageal stoma or dilating it. This led to the need for one cervical Z-plasty revision to reopen the stenosed stoma. Because of the patient's depression and intolerance of the tube, this result can only be judged fair. Nevertheless, when he used the tube, he could eat a regular diet. The patient died six months later of pneumonia.

Patient 4

A 62-year-old white woman was referred in April, 1973, after an esophagectomy followed by right colon interposition for a lye stricture had failed and a subsequent gastric tube bypass operation was unsuccessful. When first seen she had an inflamed midsternal gastrostomy opening, a jejunostomy, and a pharyngostomy. Because there was insufficient colon to attempt another bypass and because the stomach had been utilized in the gastric tube operation, she was advised that the extracorporeal tubes represented the only approach for long-term management. The stump of the gastric tube was resected and the gastrostomy tube was inserted. A cervical stoma was created to accept the Japanese tube, and the pharyngostomy was closed.

This patient has tolerated the tubes well and has eaten a regular diet for three years since the tubes were inserted. She has gained 16.75 kg above her admission weight. Three revisions of the cervical stoma have been necessary, partly because of neck scarring from the previous pharyngostomy and earlier neck explorations.

Patient 5

A 64-year-old white man was referred in January, 1974, after a Collis gastroplasty and resection of a reflux stricture with left colon interposition had failed. He was evaluated for a possible further reconstructive procedure. Because of a previous colon resection in addition to the attempted colon interposition and because the stomach had been utilized for the gastroplasty, we advised him that the extracorporeal tubes were the only approach for long-term management. These were inserted through a revision of his esophagostomy and gastrostomy openings.

The palliation achieved has been excellent. With a regular diet his weight has increased nearly 16 kg, and he has resumed normal activity during a little more than two years since he began using the tubes.

Patient 6

A 71-year-old white man was referred in November, 1974, for treatment of squamous cell carcinoma of the middle third of the esophagus. Because of involvement of the trachea, resection was not attempted. Radiation therapy was instituted, but a tracheoesophageal fistula developed. The patient refused the offered colon bypass operation and agreed to have the gastrostomy and esophagostomy tubes inserted. At laparotomy the cardia was divided completely and closed. The gastrostomy tube was inserted. The cervical esophagus was transected and a stoma was created; this was in the field of radiation therapy, and healing was delayed. One cervical Z-plasty was required.

Eventually the patient developed an excellent result with the tubes. The course of radiation therapy was completed. He has maintained his weight and taken a regular diet for more than sixteen months since his tracheoesophageal fistula developed. At present the fistula measures approximately 6 cm, and the esophagus, closed at both ends, is like a diverticulum on the trachea.

Comment

Complications of therapy for carcinoma were the primary indication for the external esophagogastric tube in 4 of the 6 patients; in the other 2 the tube was used following failure of several operations for benign stricture. A summary of indications, results, and follow-up is presented in the Table. Because of the annoyance to the patient and the need for continuing care of the stomas, this procedure is employed only when other types of permanent

Indications for and Results with the Esophagogastric Tube

Patient No.	Indication	Result	Stoma Revision	Follow-up
1	Infarcted L colon bypass, esophagectomy & radiotherapy	Excellent	1 Cervical	Dead 15 mo; 10.4 kg weight gain
2	Infarcted R colon bypass, esophagectomy & radiotherapy	Poor	None	Dead 12 mo; stump too short
3	T-E fistula during radiotherapy	Fair, when used	1 Cervical, 1 gastrostomy	Dead 6 mo; weight stable
4	Failed R colon interposition, failed gastric tube bypass	Excellent	3 Cervical	Well 34 mo; 16.75 kg weight gain
5	Failed Collis gastroplasty, failed L colon interposition	Excellent	None	Well 25 mo; 15.85 kg weight gain
6	T-E fistula during radiotherapy	Excellent	1 Cervical	Well 16 mo; weight stable

T-E = tracheoesophageal.

esophageal reconstruction are unavailable or are refused by the patient. The operation itself is relatively simple and of low risk compared with other types of esophageal replacement. Nevertheless, the patient must make a great investment in the care of the tubes and must have sufficient optimism and enthusiasm to make them work. Provided that the cervical stump is long enough, a successful outcome depends on the patient's commitment to achieving a good result.

Another difficulty encountered with this approach is availability of the tubes. Because the market for these devices is small, we have been unable to date to interest an American manufacturer in developing them. They are available from Japan, and delivery generally takes four months following submission of an order.

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Notice from The Society of Thoracic Surgeons

Call for Abstracts—1977 Meeting
(Deadline: September 15, 1976)

Abstracts for papers to be presented at the 1977 Annual Meeting of The Society of Thoracic Surgeons are now being accepted. The meeting is to be held at the San Francisco Hilton Hotel, San Francisco, California, January 24–26, 1977.

The deadline for receipt of abstracts is September 15, 1976. An original and eight copies should be submitted to F. G. Pearson, M.D., Chairman, Program Committee (Abstracts), The Society of Thoracic Surgeons, 111 E Wacker Dr, Chicago, IL 60601. Abstracts must summarize an original contribution not presented or submitted elsewhere. Abstracts received after the deadline will not be considered. It is requested that the covering letter indicate the author who is to receive notice of acceptance or rejection and the author who will present the paper.

The Program Committee reserves the right to select papers for either regular or forum-type presentation. The author may also designate his preference for presentation in the forum. Essayists are reminded that the complete manuscript must be submitted in duplicate either to the Editor of *The Annals of Thoracic Surgery* before the meeting or to the Secretary of the Society at the meeting, immediately prior to presentation.

Call for Surgical Films
(Deadline: September 15, 1976)

The popular surgical movie program will again be presented at the San Francisco meeting. The Program Committee hereby solicits the submission of surgical films, which may portray a surgical procedure or simply a technical maneuver that the surgeon thinks will be of interest to the Society. The film may not exceed 10 minutes in length. Sound movies are acceptable but not necessary, and live narration by the principal surgeon is a requirement for participation in the movie night program. The movies may be on Super-8 or 16-mm film. The deadline for submission of films is September 15, 1976. Films also should be sent to F. G. Pearson, M.D., Chairman, Program Committee, at the Society office, 111 E Wacker Dr, Chicago, IL 60601.

Application for Membership
(Deadline: September 1, 1976)

Requests for membership application forms should be addressed to Charles R. Hatcher, M.D., Chairman, Membership Committee, The Society of Thoracic Surgeons, 111 E Wacker Dr, Chicago, IL 60601.

The completed application forms and supporting letters must be in the hands of the Membership Committee by September 1, 1976, for the applicant to be considered for election at the San Francisco meeting next January.

Thomas D. Bartley, M.D.
Secretary

Repair of Inflammatory Tracheoesophageal Fistula

Hermes C. Grillo, M.D., Ashby C. Moncure, M.D., and M. Terry McEnany, M.D.

ABSTRACT **Benign acquired tracheoesophageal fistula is uncommon. Erosion of the membranous wall of the trachea and the anterior esophageal wall by the high-pressure cuff on a tracheostomy tube, often against the anvil of a nasogastric tube, may produce such fistulas. Techniques for closure have included patching the tracheal defect with muscle and, often, multiple staged procedures, planned or unplanned.**

Since any cuff lesion severe enough to cause a fistula necessarily damages the trachea circumferentially at the same level, definitive correction must include circumferential tracheal resection as well as closure of the fistula. Five patients with tracheoesophageal fistula due to cuff perforation had repair by such a single-stage procedure. Through an anterior approach the involved trachea was resected, primary anastomosis was done, and the esophagus was closed in layers. In 3 of these 5 patients muscle was interposed for added security. One patient had undergone a prior attempt at repair elsewhere. One required a second resection of trachea for subsequent stomal stenosis. Repair in 2 additional patients with fistulas of complex origin related to direct trauma, sepsis, and foreign body involved adaptation of the basic technique to the special problem; 1 of these procedures was necessarily staged. Results in all 7 patients have been good.

Tracheoesophageal fistula is a fairly uncommon but often disastrous lesion that has appeared with the increasingly frequent use of ventilatory assistance with cuffed tubes. In 1968, in a review of acquired nonmalignant esophagotracheal and esophagobronchial fistulas, Wesselhoeft and Keshishian [19] reported no cases of tracheoesophageal fistula related to cuffs. In 1973 Thomas [17] collected 46 such cases, 30 of them fully documented, including 7 patients of his own. All reports of spontaneous cures were in unproved cases. Eight of 11 patients with proved fistulas who had attempts at surgical repair survived. A variety of procedures have been employed in treatment [2, 4, 10, 11, 16]. Some have been staged operations, either by plan or in effect, in which tracheal stenosis after repair of the tracheoesophageal fistula has required further treatment.

In pressure necrosis from a cuff that results in tracheoesophageal fistula, the pressure is exerted circumferentially; therefore most of these patients have significant circumferential damage to the trachea. Late tracheal stenosis may usually be anticipated even if the fistula is closed in an initial procedure. We therefore prefer, when possible, to perform a single-stage procedure directed at correcting both the tracheal and the esophageal disorders. This procedure consists of closure of the esophageal fistula and circumferential resection and reconstruction of the damaged segment of trachea. Five patients with tracheoesophageal fistula due to cuff perforation underwent repair by such a single-stage procedure. Two additional patients with tracheoesophageal fistula of complex origin had repair that involved adaptation of the basic technique to their special problems. One required staging.

Such repair of a tracheoesophageal fistula originating from cuff pressure should be done only after the patient has been weaned from mechanical respiratory assistance. Anesthesia and operation should be conducted so as to avoid the need for postoperative ventilatory support. If repair must be done prior to weaning, techniques which defer tracheal reconstruction are probably preferable [1].

Technique of Operation

Since most of these patients have a tracheostomy tube in place, induction of anesthesia is easily done by inhalation technique with halothane. Bronchoscopy and esophagoscopy are both

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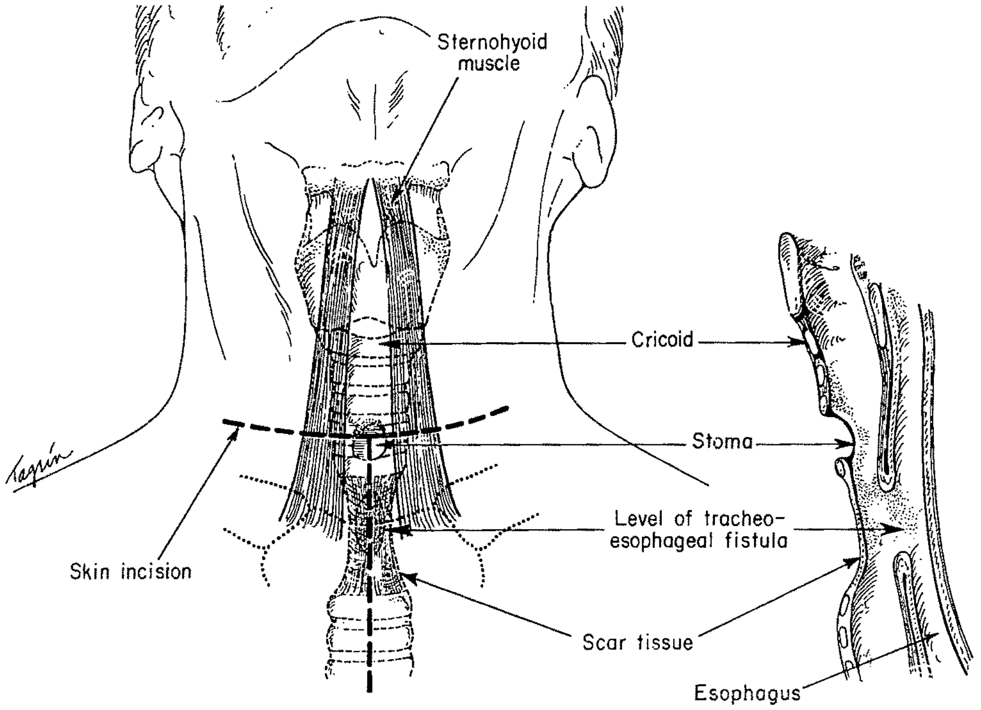
necessary for delineation of the fistula. Oral intubation is done next, with the tube positioned so that its cuff will effectively seal the fistula. A nasogastric tube is inserted and placed on suction. A low collar incision is preferable for the initial exploration, with a vertical extension downward over the upper sternum if additional exposure is needed (Fig 1). The approach and method of dissection are those which we employ in the surgical management of tracheal stenosis [6–8].

The anterior surface of the trachea is freed from the cricoid cartilage to the carina. Dissection is carried lateral to the trachea at the level of the fistula to expose this area and the esophagus (Fig 2A). The trachea is circumferentially dissected immediately below the fistula. The posterolateral margins of the trachea are freed distally no more than 1 or 2 cm below the estimated point where the distal trachea will ultimately be divided, in order to avoid devascularization of the distal trachea. If dissection is kept close to the trachea, the fistula, and the esophagus, there is no need to isolate or identify the recurrent laryngeal nerves; indeed, in scar tissue there is a hazard in doing so. The lateral dissection is carried a short distance above the level of the fistula. The stoma is usually contiguous to the injured segment of trachea containing the fistula. If there is difficulty in establishing the level of the fistula, bronchoscopy is done intraoperatively through either the patient's mouth or the stoma.

Following transection of the distal trachea and intubation across the operative field, the proximal damaged portion of the trachea is drawn upward. The esophagus is entered just below the lowermost border of the fistula, and elliptical excision is begun (Fig 2B). It is not always necessary to dissect the esophagus completely from its bed, but adequate mobilization should be achieved so that closure will be free from tension. The line of excision is carried upward on both sides until the upper border of the esophageal portion of the fistula is reached. The trachea is dissected superiorly until a normal or relatively normal margin of airway is exposed. In some cases this will be at the cricoid cartilage. Great care must be taken to keep the dissection close to these structures in order not to damage the recurrent laryngeal nerves as they approach

Fig 1. Surgical approach to a typical lesion. The tracheal stoma lies a short distance above the area of circumferential tracheal damage caused by pressure from a cuff. In the posterior wall of the trachea, erosion has produced a tracheoesophageal fistula. The incision is shown. It may or may not be placed to include excision of the stoma.



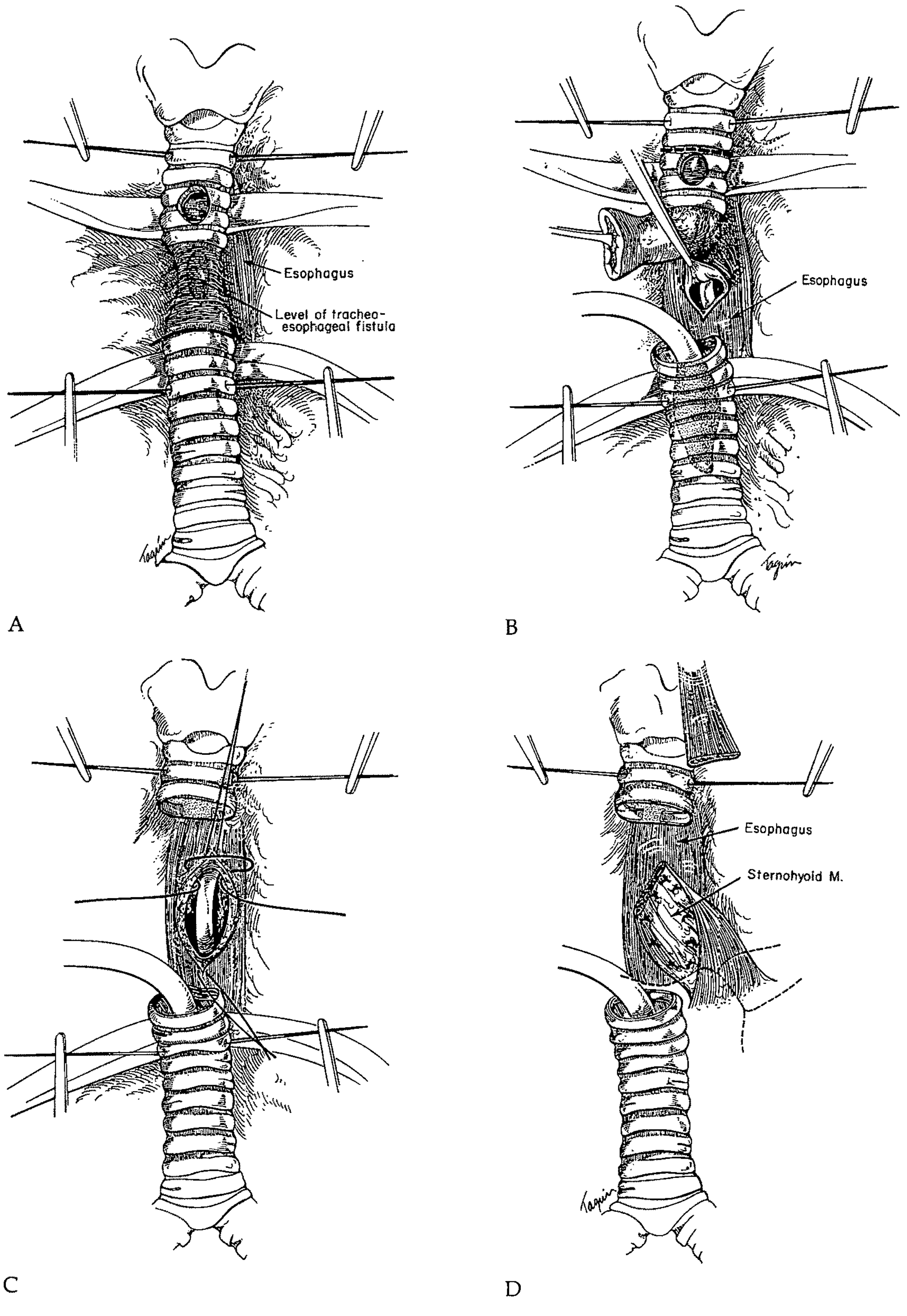


Fig 2. (A) Dissection has been carried out to expose the trachea in the midline. This dissection remains close to the trachea and esophagus in order to avoid injury to the recurrent laryngeal nerves; these nerves are not exposed. Stay-sutures are placed above and below the lines of planned resection. While it is not always necessary to resect the segment of trachea containing the stoma, this is often so close to the area of injury that the trachea below is of too poor quality to be used successfully for anastomosis. Tapes have

Data on 7 Patients Undergoing Surgical Treatment of Inflammatory Tracheoesophageal Fistula

Patient No., Age (yr), & Sex	Original Problem	Cause of TEF	Size of Fistula (cm)	Prior Attempts at Closure	MGH Repair of TEF	Incision	Amount of Trachea Excised (cm)	Management of Tracheostomy	Tissue Interposed	Postoperative Complications	Result
1. 36, M	Polyneuritis	Erosion by tracheostomy tube cuff	1	None	3/15/71	Cervical	4	Excised with trachea	None	None	Excellent
2. 59, F	Polyneuritis	Erosion by tracheostomy tube cuff	3	None	11/27/74	Cervical	3	Excised with trachea	Sternothyroid muscle	Candidiasis (responded to amphotericin)	Excellent
3. 56, F	Aortofemoral occlusive disease	Erosion by tracheostomy tube cuff	2	None	1/28/75	Cervicomediastinal	5	Excised with trachea	None	None	Excellent
4. 21, M	Head injury	Erosion by tracheostomy tube cuff	2.5	Muscle flap & dermal graft 12/6/73	3/8/74	Cervical	2.5	Allowed to close	Sternohyoid muscle	Suture line granulations requiring bronchoscopy	Excellent
5. 62, M	Mitral valve replacement	Erosion by tracheostomy tube cuff	1.5	None	3/25/75	Cervicomediastinal	2, 3	Allowed to close	None	Tracheal stenosis at stomal site requiring 3 cm resection 7/18/75	Excellent
6. 18, M	Chest injuries	Closed trauma or laceration at intubation	>2	None	9/21/73, 1/11/74 (staged)	Cervicomediastinal	0	Allowed to close	Mediastinal tissue	None	Some narrowing of esophagus
7. 29, F	Cervical disc removal & fusion	Erosion by septic bone graft	2	Divison of esophagus & muscle flap 7/31/73; colon bypass 3/3/74	7/9/75	Cervical	3.5	Excised with trachea	None	None	Excellent

the larynx posterolaterally. The decision about whether to include or exclude the tracheal stoma in the excision is made on the usual basis but is further dictated by the level of the fistula. In most cases the fistula is somewhat inferior to the level of the tracheal stoma, since a cuff caused the original injury, but in some patients it is nearly directly posterior.

been passed around the trachea above and below the fistula, but care is taken not to dissect excessive lengths of trachea circumferentially.

(B) The trachea is transected, and the patient is intubated across the operative field. With the proximal end of the divided trachea elevated, the area of the fistula can be identified. The esophagus is entered at the lowermost border of the fistula. The edges of the fistula are then excised elliptically by continuing upward on both sides (dotted lines).

(C) The trachea has been excised above the level of the stoma. Closure of the fistula in the esophagus is now begun using fine interrupted sutures that invert the mucosa. A second-layer closure is made with Lembert sutures.

(D) If it appears that the two suture lines will rest against one another, the sternohyoid or sternothyroid muscle is detached superiorly and a pedicle is inserted across the esophageal closure. This is carefully sutured into place with 4-0 silk to cover the closure completely. End-to-end tracheal repair is done by our usual technique.

We prefer Sweet's technique [15] for esophageal closure, using two longitudinal layers of 4-0 silk and inverting the mucosal layer (Fig 2C). Tracheal anastomosis is done by our usual technique [6], utilizing interrupted 4-0 Tevdek sutures placed so that the knots will be outside the lumen. None of these patients required extensive mobilization of the trachea or accessory laryngeal release procedures.

For patients in whom it appears that the vertical suture line in the esophagus and the horizontal suture line for the tracheal anastomosis will be contiguous or in whom the presence of massive inflammation causes concern, a pedicled muscle flap has been sutured over the esophageal closure prior to completion of the tracheal anastomosis (Fig 2D). The sternothyroid or sternohyoid muscle is detached superiorly and arched over the esophagus.

Clinical Experience

Data on 7 patients are given in the Table, and the lesions and their management are depicted in Figure 3. Six patients were referred from other institutions. In the first 5 the fistula had resulted

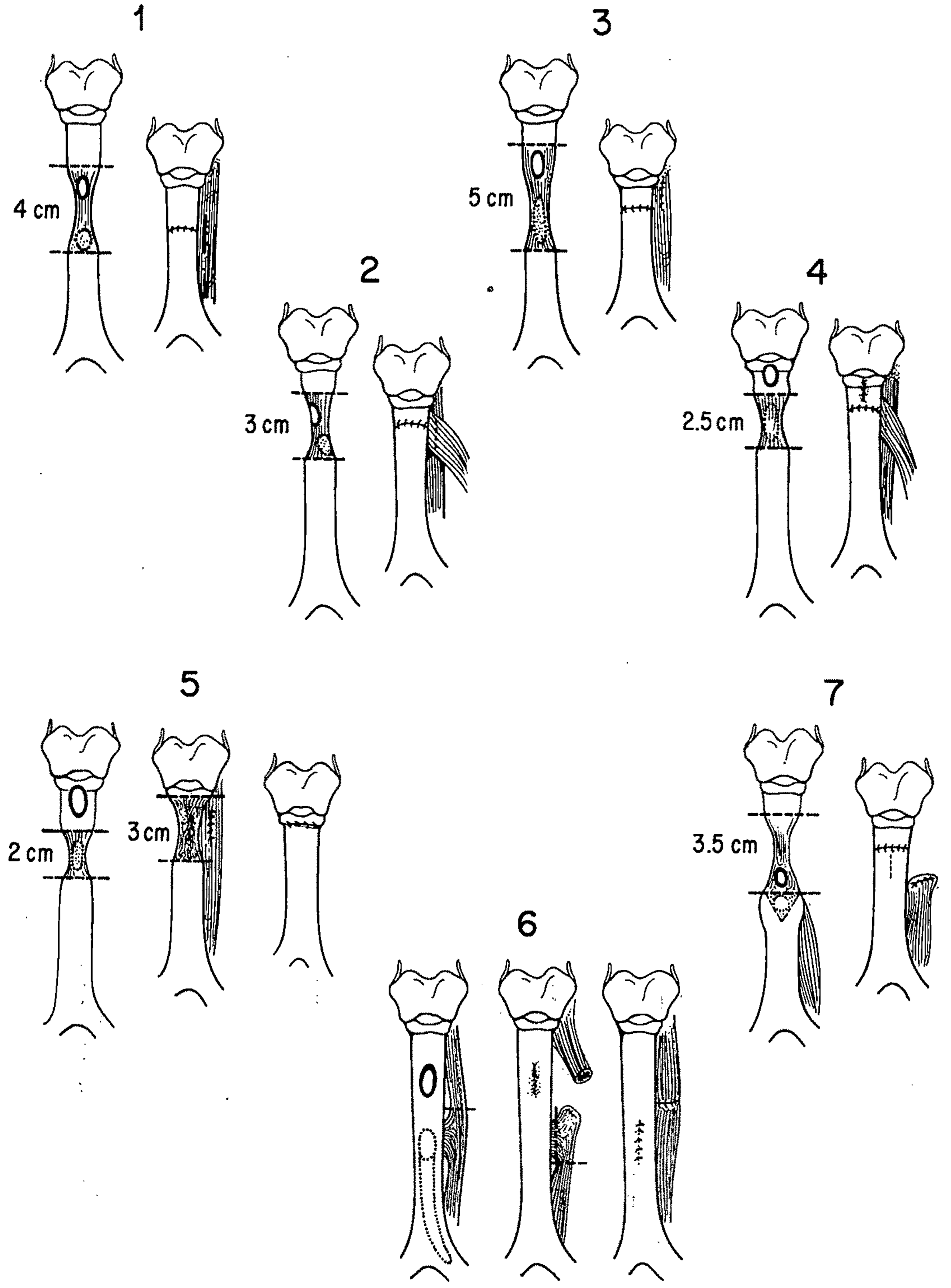


Fig 3. Lesions in the 7 patients. Both the extent of the tracheoesophageal lesion and stages of repair when more than one procedure was required are indicated. Lengths of trachea resected are noted. (Patient numbers correspond to those in the Table.)

from erosion by the cuff of a tracheostomy tube. At least 4 of the 5 had had nasogastric tubes in place for varying periods of time during ventilation. Patient 1 had a left upper lobe abscess and infiltration in other portions of his lungs. He had been managed with prolonged hyperalimentation without improvement. Patient 2 had a vital capacity of only 400 cc and required a long period of conservative management until she could tolerate repair safely. Patient 4 had had a prior attempt at closure in another hospital using a sternocleidomastoid muscle flap and a dermal graft. One recurrent laryngeal nerve was paralyzed. In the first 3 patients the tracheostomy was excised along with the adjacent injured trachea since it was in contiguity. In Patients 4 and 5 the stoma was allowed to close spontaneously after repair of the tracheoesophageal fistula. Stomal stenosis later developed in Patient 5, necessitating further resection of trachea.

Patients 6 and 7 represent variants in etiology, and their special problems required alterations in management from the straightforward approach used in the first 5 patients. Patient 6 had laceration and inflammatory injury in the lower two-thirds of the trachea, extending into the takeoff of the left main bronchus. Multiple fistulas appeared to be present on initial bronchoscopy. The injury had resulted either from his original closed chest injury or possibly from traumatic intubation. In view of the extent of the injury, it was elected to give the trachea a chance to heal as much as possible prior to repair. The esophagus was divided at an initial procedure, bringing the proximal end out as a cervical stoma. The distal esophagus was closed just above the fistula. Three months were allowed for regression of inflammation. At the definitive operation it was possible to close the membranous wall of the trachea longitudinally since the original injury had not been of the circumferential type caused by a cuff. The fistula was excised, and end-to-end repair of the esophagus was performed. The tracheal stoma was allowed to close between the stages since it was no longer needed.

The fistula in the seventh patient had resulted from erosion by a septic bone graft placed following a cervical disc operation with fusion. The patient had previously undergone division of the esophagus with interposition of a muscle flap. This had failed, and colon bypass had been performed. At the final operation we excised the segment of stenosed trachea and the adjacent stoma. This was not a cuff lesion, and the fistula to the distal esophageal stump lay below the level of stomal stenosis in a dilated trachea. In view of the length of the tracheal segment excised above, the fistula was removed with a V-shaped piece of membranous wall. Thus the tracheal repair consisted of a circumferential end-to-end repair, but there was a vertical T inferior to the circular suture line posteriorly.

Specific operative complications were few. One patient developed candidiasis, possibly due to her general state of nutrition and possibly following erosion of a subclavian line into the pleural space. She responded to a course of amphotericin. One patient developed suture line granulations that had to be removed bronchoscopically. Since then, his anastomosis has been excellent. Reference has already been made to a patient who developed stomal stenosis necessitating resection of an additional 3 cm of trachea, with an excellent result. Patient 6 developed narrowing of the esophageal anastomosis and required dilation. He appeared to have slight dysphagia for solid food, but he rejected further dilation.

Comment

Numerous authors [4, 9–12, 14, 17, 18] have called attention to the occurrence of tracheoesophageal fistula due to pressure by the inflated cuffs of tracheostomy tubes. The pathological evolution of such injury has been made clear by Cooper and Grillo [3] and by Florange, Mueller, and Forster [5]. Compression of the membranous wall of the trachea and the esophageal wall between a high-pressure cuff and a nasogastric tube appears to be an important factor in production of these fistulas.

The principal thesis of this report is that benign acquired tracheoesophageal fistulas are usually best managed by a single-stage, definitive operation that corrects the fistula and also removes concurrent tracheal disease. It is directed primarily toward the problem of tracheoesophageal fistula resulting from intubation, most often due to circumferential necrosis by a high-pressure tracheostomy tube cuff. With such lesions, later stenosis is almost inevitable, and excision of the involved trachea is best performed as part of the corrective procedure. The evolution of tracheal surgery [8] has been such that this does not present added hazards to the patient if performed by an experienced surgeon.

Surgical experience with this particular variety of tracheoesophageal fistula has not been great, so even a small series such as ours has validity. We have included 2 additional cases to augment the experience and to illustrate the need for varying the technique, in accordance with the principles stated, to deal with specific problems.

Scattered attempts at repair of cuff-induced tracheoesophageal fistula have been reported [2, 4, 10, 11, 16], with a few successes. Prior surgical experience supports the wisdom of repairing the trachea at the time of the initial operation. Of Thomas' [16] 7 personal cases, 2 patients died without operation and 1 was awaiting operation at the time of death. The other 4 had the esophageal portion of the fistula sutured, but the tracheal opening was closed with a muscle flap. One of them died eight days postoperatively. Of the remaining 3, 2 developed tracheal stenosis. One was treated with later resection of the stenosis and 1 by repeated dilations without clear-cut resolution at the time of the report. One of the 2 patients presented by LeBrigand and Roy [10] developed tracheal stenosis.

A lateral approach has been used most often in the past. Our standard anterior approach [6] to tracheal reconstruction offers several advantages when applied to the problem of tracheoesophageal fistula: exposure of the fistula is bilateral; the recurrent laryngeal nerves are less likely to be injured; both trachea and esophagus are exposed with a single route of dissection; and, when high resection is necessary, the thyroid gland is out of the way. Olivet and Payne [13] described repair of a congenital H-type tracheoesophageal fistula by closure of the esophageal defect and segmental removal of the trachea with this approach. In the past, the more complicated nature of inflammatory disease has probably inhibited application of the technique proposed here to acquired fistulas.

The method described should be used in patients no longer having respiratory support. If weaning cannot be accomplished and the fistula remains uncontrolled, patching techniques with or without esophageal diversion are probably in order [1].

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Discussion

DR. ARTHUR N. THOMAS (San Francisco, CA): We have had experience with a total of 9 patients who had tracheoesophageal fistula from cuffed tubes. Seven were treated surgically.

I am concerned about using tracheal resection and anastomosis as the primary approach in these severely ill patients. In some situations it would be impossible or hazardous. One of our patients had thirteen tracheal rings involved. An associated mediastinal abscess may exist in 10 to 20% of the patients. Tracheal cartilages adjacent to the fistula are often eroded. Most of these patients have tracheobronchial sepsis and respiratory failure. One-third of tracheoesophageal fistulas occur in patients who have had neurosurgical procedures, and often the fistula is treated with systemic steroids that impair wound healing. All these situations increase the risk of primary anastomosis at the time of treatment of the tracheoesophageal fistula.

Dr. Grillo indicates that the patient should be weaned from mechanical ventilation before tracheal resection is undertaken. This course would often lead to a delay before closure of the fistula was accomplished. Often, respiratory insufficiency and the need for mechanical ventilation exist because of the fistula and repeated aspiration. We advocate early closure of the fistula by the simplest method possible. Delay in operative closure of a fistula risks enlargement or massive aspiration. We regretted delaying treatment in 4 of our patients, as 2 of them died without having an operative repair. Extensive tracheoesophageal fistulas are almost invariably the result of late treatment. Fistula enlargement occurs as the tube cuff is progressively advanced toward the carina in an attempt to obtain an air seal.

Although two-thirds of the patients reported to have survived repair of tracheoesophageal fistula have subsequently developed tracheal stenosis at the level of either the stoma or the fistula, one-third have not. In our 7 operated patients, 2 developed stenosis; 1 of them required resection. After fistula repair, one can watch for tracheal stenosis and treat this electively if it occurs.

Finally, I would anticipate that if tracheal resection and anastomosis were done in the acute stage, there would be errors in delineating the extent of involved trachea. Whether stenosis will occur may not be clear until weeks after decannulation. Since the mortality among patients with fistulas resulting from cuffed tracheal tubes is 70 to 80%, I believe treatment should focus on a simple means to close the fistula and isolate the gastrointestinal tract from the airway.

DR. GRILLO: I don't think Dr. Thomas and I have expressed a fundamental difference of opinion. I very carefully attempted to confine my discussion to those patients who are able to be weaned from a respirator. Obviously, one does not simply discard the ones who cannot be weaned. It is a very complex subject, and perhaps giving a paper about a selected group makes it seem too simple. These problems require fine judgment all along the line. Some patients who no longer need respiratory support have really extensive lesions, and other approaches must be taken; 1 of the patients I presented indicated just that. A few patients will not require circumferential resection, and 1 of my cases demonstrated that. One must apply the appropriate procedure to the individual patient.

As for those patients still on a respirator—an even more complicated topic—if I were to discuss that, I should need to write another paper. Dr. Thomas alluded to the principal points. Several of the patients reported were receiving respiratory support when we first saw them. In our judgment, we could get them off the respirator and therefore it was safer to wait and do elective procedures. After this kind of delay, the majority of cuff lesions will turn out to have tracheal stenosis as well.

I certainly agree that it is a complex problem with complex variations, and I do not want to leave the impression that every tracheoesophageal fistula from a cuff should be handled by one standard approach, without any sort of judgment being used in each individual case.

Gastroesophageal Reflux in Esophageal Scleroderma: Diagnosis and Implications

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Chris J. D. Zarafonetis, M.D., and Herbert Sloan, M.D.

ABSTRACT **Fifty-three patients with scleroderma were evaluated by history, barium swallow, and esophageal function tests. The most common esophageal symptoms were heartburn and dysphagia. Abnormal motility was seen radiologically in 43 patients, gastroesophageal reflux in only 9. Esophageal function tests demonstrated: (1) abnormal motility in 51 patients and lack of a distal esophageal high-pressure zone in 18; (2) moderate to severe gastroesophageal reflux in 38; and (3) abnormal acid-clearing ability in 50.**

Eleven patients, including 8 with peptic stricture, underwent the combined Collis-Belsey operation. Symptomatically, reflux was abolished in all and dysphagia in 10. Roentgenograms showed that regression of strictures was complete in 5 and partial in 3. Postoperative esophageal function tests in 9 patients demonstrated a competent distal esophageal valvular mechanism in 7.

Gastroesophageal reflux, not impaired motility, is the major cause of esophageal symptoms in scleroderma. Its effective operative control is not contraindicated by systemic disease in these patients.

Systemic scleroderma is a disease of unknown etiology characterized by induration of the skin, fibrous replacement of the smooth muscle of internal organs, and progressive loss of visceral and cutaneous function [41]. Disruption of normal esophageal peristalsis is so common in scleroderma that it is recognized as a major diagnostic sign of the disease. As fibrous replacement of esophageal smooth muscle progresses, the distal esophageal high-pressure zone (HPZ) loses its tone and normal response to swallowing. The resultant gastroesophageal reflux, coupled with the impaired ability of the atonic lower esophagus to clear refluxed gastric contents back into the stomach, sets the stage for the development of reflux esophagitis.

In scleroderma, for which there is currently no consistently effective treatment, the esophageal symptoms are typically treated symptomatically and strictures are dilated when they occur [26]. A small number of authors have advocated surgical treatment of the esophageal abnormality in these patients [6, 16, 30]. Most, however, have considered the risk of hiatal hernia repair, esophagomyotomy, or distal esophagectomy and reconstruction too great in the face of a disease which is systemic. Henderson and Pearson [16] have recently emphasized the importance of gastroesophageal reflux in patients with scleroderma and esophageal symptoms. In addition, they demonstrated in these patients the satisfactory results that can be achieved by combining the Collis gastroplasty with the Belsey Mark IV hiatal hernia repair, which they first proposed as treatment for dilatable peptic esophageal strictures [31].

This study was undertaken to define precisely the pathophysiology of esophageal involvement in scleroderma and to evaluate the place of surgery in the management of gastroesophageal reflux in these patients.

Material and Methods

During the past two years the esophageal function of 53 consecutive, unselected patients with scleroderma has been evaluated at the University of Michigan by history, radiological examination, and esophageal function tests. Forty-three patients with established scleroderma were studied to document esophageal involvement. Nine were examined as part of our routine evaluation of patients with Raynaud's phenomenon or symptoms suggestive of scleroderma, and the diagnosis was subsequently established. Esophagoscopy was performed in 19 of

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these patients, including the 11 who subsequently underwent operation.

Esophageal function tests in all patients included manometry, measurement of acid reflux, evaluation of acid clearing, and the acid-perfusion test. Intraesophageal pressures were measured through triple-lumen catheters with openings spaced 5 cm apart, through which normal saline was constantly perfused at a rate of 1.7 ml per minute. The recording catheter was inserted through the nose and into the stomach with the patient supine. With a pneumograph device around the abdomen to monitor respirations, the assembly was withdrawn at 1 cm increments as pressures were recorded simultaneously with a Grass recorder from each of the three openings. Multiple pullback tracings of the resting-pressure profile for the gastroesophageal junction were recorded, and the mean and peak pressures in the distal esophageal HPZ were determined for each subject by averaging the highest values of three to five replications. The overall mean and the standard deviation of these mean values were determined. The responses of the esophagus and its sphincters to deglutition were recorded.

As suggested by Garrett and his associates [12], the degree of esophageal involvement with scleroderma, as indicated by abnormal manometric determinations, was defined as mild, moderate, or severe. Mild involvement was characterized by varying strength of contractions after deglutition; some responses to swallowing were normal and others were weak and simultaneous. With moderate involvement, esophageal contractions after swallowing were generally weak or incoordinated. Lack of esophageal contractions after deglutition throughout the smooth muscle portion of the esophagus indicated severe involvement.

Acid-reflux testing was performed as described by Kantrowitz and his associates [17] by placing 300 ml of 0.1 N HCl into the stomach and monitoring intraesophageal pH with an electrode positioned 5 cm above the HPZ, or the pressure-inversion point when no HPZ was present. Intraesophageal pH was recorded with the patient breathing quietly and deeply, performing Valsalva maneuvers, and coughing while supine, on the right side, on the left side, and in the 20-degree head-down position. A drop of the intraesophageal pH below 4 was interpreted as an episode of reflux, which was graded as minimal (1+) if there were one or two transient drops in pH during the entire sequence, moderate (2+) if there were more frequent falls in pH, and severe (3+) if intraesophageal pH remained low or if there were multiple episodes of reflux during the study.

Acid-clearing ability was tested with a 15 ml bolus of 0.1 N HCl placed into the esophagus through the recording catheter while intraesophageal pH was being continuously monitored [4]. The number of swallows at 15-second intervals required to raise the pH to 5 was recorded. Acid clearing was considered normal if the bolus of acid was cleared in ten swallows or less.

The acid-perfusion (Bernstein) test [3] was performed with the patient in the sitting position while a constant intraesophageal infusion of 0.1 N HCl was in progress at a rate of 6 ml per minute for 10 minutes. The test was considered positive if the patient's esophageal symptoms were reproduced with acid perfusion and abolished by changing to a saline perfusion.

Results of Clinical Evaluation

Esophageal symptoms were present in 48 of the 53 patients (Table 1). Twenty-four complained of slow emptying of the esophagus and had to drink large amounts of fluids with meals to wash food through their atonic esophagus. In 19 this was the initial esophageal complaint, occurring

Table 1. Esophageal Symptoms of Scleroderma (53 Patients)

Symptom	No. of Patients	Percent
Heartburn with postural aggravation	36	68
Substernal dysphagia	27	51
Regurgitation	26	49
Delayed emptying	24	45
Reflux to throat	23	43
Cervical dysphagia	17	32
Chest pain	13	25
Nocturnal aspiration	11	21
Cough with swallowing	6	11

Table 2. Barium Swallow Findings in Scleroderma (53 Patients)

Abnormality	No. of Patients	Percent
Diminished primary peristalsis	43	81
Dilatation	26	49
Hiatal hernia	17	32
Stricture	13	25
Delayed emptying	10	19
Gastroesophageal reflux	9	17

before the onset of symptoms of gastroesophageal reflux.

The barium swallow findings in these patients are shown in Table 2. Distal esophageal strictures and hiatal hernias were each present in approximately one-quarter of the patients. In only 9 patients was gastroesophageal reflux documented by roentgenographic examination.

Esophageal function tests proved to be the most sensitive indicator of esophageal abnormality (Table 3). In one-third of the patients there was complete loss of tone of the distal esophageal sphincter mechanism with no identifiable HPZ (Fig 1). Only 2 of the patients had no demonstrable motility disorder. Forty-one had moderate to severe sclerodermal involvement of the esophagus as determined by manometry (Fig 2). Moderate or severe acid reflux was documented in 38 of these patients (Fig 3). Acid-clearing ability was abnormal in 50 patients. In 37, instillation of acid into the esophagus produced no symptoms.

Of the 19 patients who underwent esophagoscopy, gastroesophageal reflux was seen in 18. Three had Grade I esophagitis (mucosal erythema); 6 had Grade II esophagitis (mucosal erythema plus superficial ulceration); and 9 had an esophageal stricture (Grade III esophagitis). One patient had a distal esophageal ring without evidence of reflux esophagitis.

Surgical Treatment

Eleven patients, including 8 women and 3 men ranging in age from 31 to 70 years (average, 47 years), underwent combined Collis-Belsey re-

Table 3. Results of Esophageal Function Tests in Scleroderma (53 Patients)

Test	Finding	No. of Patients	Percent
Manometry			
Characteristics of HPZ (mean ± SD)			
Mean pressure (mm Hg)	3.02 ± 2.69		
Peak pressure (mm Hg)	8.34 ± 4.65		
Length (cm)	1.83 ± 1.65		
No HPZ		18	34
Motility disorder			
None		2	4
Mild		10	19
Moderate		24	45
Severe		17	32
Acid-reflux test			
Negative		11	21
Minimal (1+)		4	8
Moderate (2+)		4	8
Severe (3+)		34	64
Acid-clearance test			
Abnormal		50	94
Normal		3	6
Acid-perfusion test			
Positive		16	30
Negative		37	70

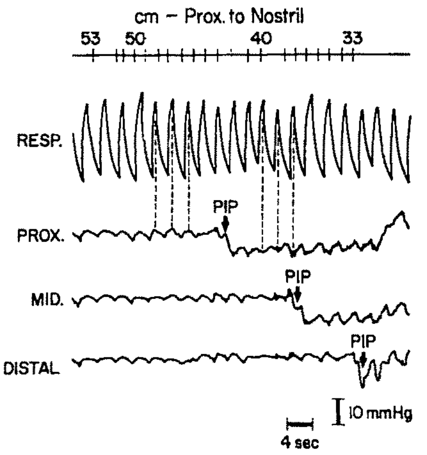


Fig 1. Preoperative pullback resting-pressure profile of the gastroesophageal junction in a patient with scleroderma (same patient as in Figures 3, 4, and 5). Note the lack of a distal esophageal high-pressure zone. The pressure-inversion point (PIP) occurs at 42 cm from the nostrils. Distal to this point there is an intraabdominal pressure pattern, with peak intraluminal pressures occurring at the height of inspiration. Proximal to this point, within the thorax, intraesophageal pressures are negative at the peak of inspiration. For subsequent acid-reflux testing the intraesophageal pH probe is positioned 5 cm proximal to the PIP.

construction of the esophagogastric junction as described previously [28]. The indication for operation in each case was symptomatic reflux esophagitis refractory to medical management; 8 of these patients had esophageal stricture and 3 had Grade II esophagitis at endoscopy. Three patients had undergone a total of seven previous operations, five transthoracic and two transabdominal, to control gastroesophageal reflux. In all 3, symptoms of heartburn and regurgitation had recurred within weeks to months after each operation.

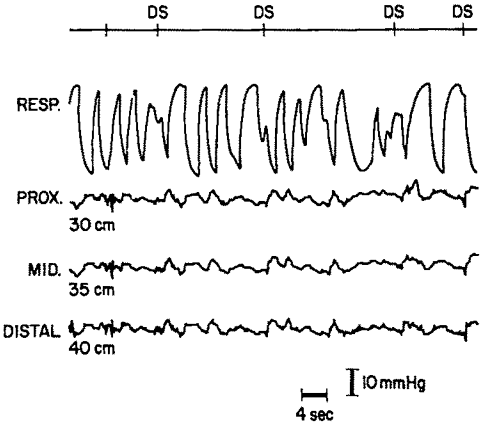


Fig 2. Aperistalsis in esophageal scleroderma. There is a lack of effective peristalsis with swallowing in the distal esophagus. (DS = dry swallow.)

Additional procedures performed at the time of the combined Collis-Belsey repair included dilation of a peptic stricture (8 patients), lung biopsy (5 patients), pyloroplasty or pyloromyotomy (3 patients), and gastrostomy (2 patients). The average hospitalization after operation was 11 days. The only complication was deep thrombophlebitis of the leg in 1 patient that necessitated anticoagulant therapy.

Each patient in whom intraoperative dilation of a peptic stricture was performed had calibration with a 50F Hurst-Maloney esophageal dilator prior to discharge from the hospital. Dilation was repeated on an outpatient basis at 2 weeks and 1 month postoperatively and then was not performed again unless there was persistent or recurrent dysphagia.

Results of Surgical Treatment

The duration of follow-up for these 11 patients ranges from 3 to 15 months (average, 10.2 months). All have had postoperative barium swallow examinations showing anatomical reduction of the hiatal hernia, if present preoperatively, and a 3 to 5 cm segment of intraabdominal distal "esophagus." In only 1 patient was reflux demonstrated postoperatively by radiological examination. Regression of esophageal strictures, as demonstrated roentgenographically, has been complete in 5 patients and partial in 3 (Fig 4).

Nine patients have had follow-up esophageal manometric examinations and acid-reflux testing 3 to 6 months after their operations. In 8 these studies were repeated again at least one year postoperatively. Preoperatively 5 of these patients had had no measurable distal esophageal HPZ (see Fig 1). Postoperatively, all patients had a definable area of increased pressure in the distal esophagus (Fig 5). Although not statistically significant because of the small number of patients, the average mean and peak pressures in the HPZ more than doubled, from 2.22 ± 2.95 mm Hg to 5.00 ± 1.73 and from 4.44 ± 5.88 mm Hg to 10.56 ± 3.88, respectively. The average length of the HPZ increased from 1.11 ± 1.54 cm to 2.67 ± 0.50 cm. Preoperatively, 8 of the 9 patients had massive (3+) gas-

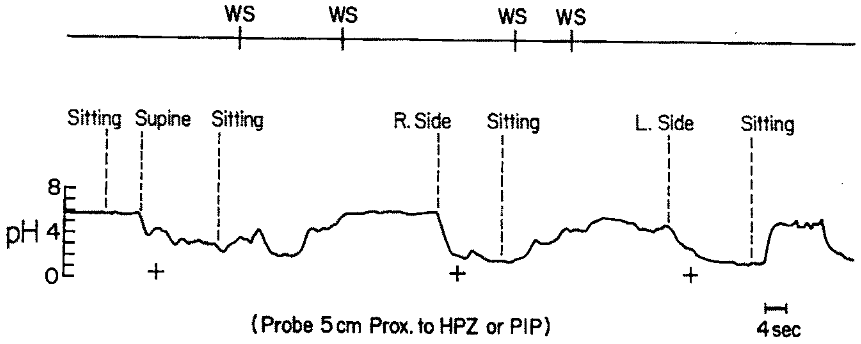


Fig 3. Strongly positive (3+) preoperative acid-reflux test (same patient as in Figures 1, 4, and 5). Gastroesophageal reflux (+), indicated by drops in intraesophageal pH below 4, occurs whenever the patient lies supine, on the right side, or on the left side. (WS = *wet swallow;* HPZ = *high-pressure zone;* PIP = *pressure-inversion point.)*

troesophageal reflux on acid-reflux testing (see Fig 3); 1 had moderate (2+) reflux. Postoperatively, acid reflux was absent in 6 patients (Fig 6), minimal (1+) in 1, moderate (2+) in 1, and severe (3+) in 1. In each of these last 2 patients, persistent or recurrent gastroesophageal reflux was present at the time of their first postoperative evaluation by manometry and acid-reflux testing 3 months after operation, despite roentgenographic evidence of a 3 to 5 cm length of intraabdominal distal "esophagus." In all 11 patients—even those with measurable acid reflux—symptoms of gastroesophageal reflux have been abolished, and the ability to swallow a regular diet, including such foods as meat and bread, has been restored. This relief from dysphagia has been dramatic and gratifying in each case. Only 1 patient has had mild intermittent substernal dysphagia and has required repeated esophageal dilations postoperatively.

Comment

Because the etiology of scleroderma remains obscure, specific curative therapy is not yet possible. Although death from cardiac, renal, and pulmonary involvement in these patients is common, five-year survival from the time of initial diagnosis varies from 33 to 70% [24, 40] so that many require prolonged medical management. Control of Raynaud's phenomenon and the vascular changes of scleroderma with vasoactive drugs and the use of antiinflammatory and antifibrotic agents [42] to reduce sclerosis are among the more commonly accepted modes of therapy. Esophageal symptoms in scleroderma, however, can constitute the most incapacitating and difficult to treat aspects of the disease.

Since the earliest reports of involvement of the esophagus in scleroderma [11, 13, 33, 34], emphasis has been placed upon the predominant motor abnormality associated with atrophy of the esophageal smooth muscle. Roentgenographic studies have demonstrated the typical dilatation, loss of primary peristalsis, impaired motility, and delayed emptying of the esophagus in these patients [5, 14, 21–23, 26]. The development of esophageal manometric examination has provided more graphic demonstration of the impairment or absence of esophageal peristalsis [10, 18, 19, 25, 35, 38] and, in addition, has revealed loss of lower esophageal sphincter tone and the ability to relax normally with deglutition in many patients with scleroderma [7, 8, 39].

Whereas disordered esophageal motility in scleroderma has been well recognized, the high incidence of associated gastroesophageal reflux has not received the same attention [32]. Roentgenographic studies have generally focused upon the motility disorder, occasionally noting an associated hiatal hernia [15, 26, 37], but more often they have completely excluded mention of either hiatal hernia or gastroesophageal reflux [14, 20]. When the extra effort has been made, however, the radiological demonstration of reflux in these patients has been common [1]. In our 53 patients with scleroderma, roentgenographic evidence of hiatal hernia was reported in 17, stricture in 13, and gastroesophageal reflux in only 9 patients.

With increasing awareness of the limitations

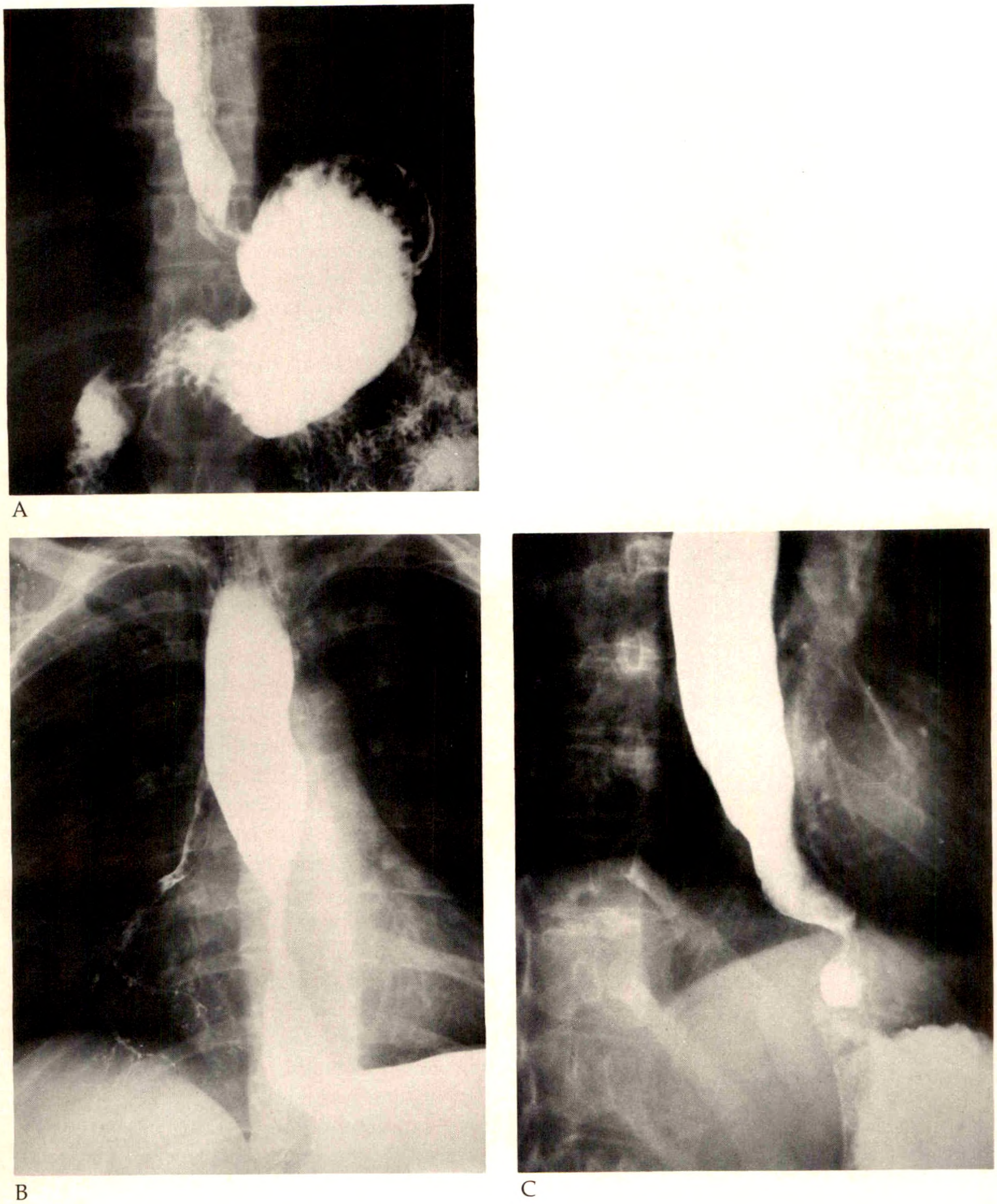


Fig 4. Barium swallow examinations in a patient with scleroderma (same patient as in Figures 1, 3, and 5). (A) Normal study (1969). (B) Study showing esophageal dilatation proximal to a stricture, with aspiration of barium into right middle lobe secondary to the obstruction (1974). No gastroesophageal reflux was seen fluoroscopically. The patient had massive (3+) reflux on her acid-reflux test. (C) Postoperative study after one year shows regression of the stricture. The subdiaphragmatic gastroplasty tube is compressed by the fundic wrap.

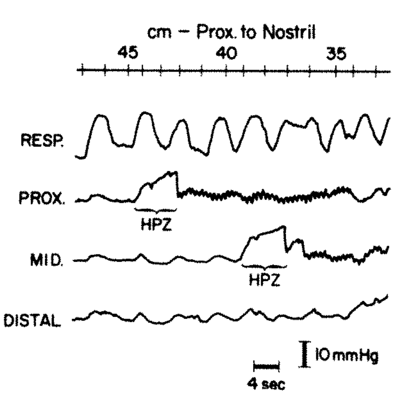


Fig 5. Pullback resting-pressure profile of the gastroesophageal junction following a Collis-Belsey operation (same patient as in Figures 1, 3, and 4). Note the presence of a distal esophageal high-pressure zone (HPZ) *between 45 and 43 cm from the nostrils. Its mean and peak pressures are approximately 5 and 10 mm Hg, respectively.*

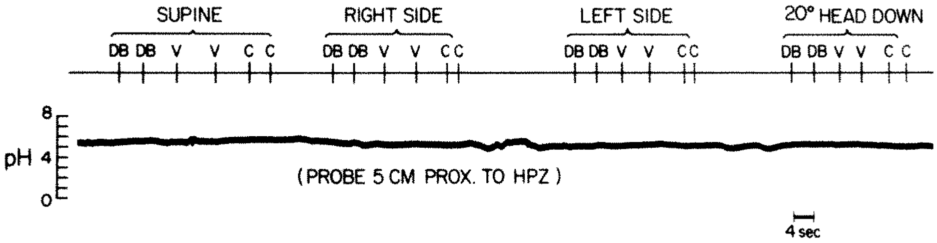
of barium swallow examination in this condition and the fact that an incompetent lower esophageal sphincter mechanism may exist even in the absence of a radiographically evident hiatal hernia, our diagnostic efforts have focused on methods which most accurately and consistently demonstrate gastroesophageal reflux. The battery of esophageal function tests performed routinely in all our patients with nonneoplastic esophageal disease includes manometry, measurement of acid reflux, evaluation of acid clearing, and the acid-perfusion test. The manometric findings of esophageal scleroderma have been described by others and were confirmed in our patients, with 41 demonstrating moderate to severe impairment of peristaltic activity and one-third showing lack of a distal esophageal HPZ. Among the 35 patients in whom an HPZ could be demonstrated, relaxation with deglutition could be shown in only 16; in 10 of these, the response was weak and intermittent. Only 6 patients showed normal relaxation of the distal esophageal HPZ with swallowing.

Skinner and Booth [36] and Benz and his associates [2] have demonstrated the efficacy of the acid-reflux test in defining abnormal gastroesophageal reflux. The finding of moderate to severe reflux in nearly three-fourths of our patients was a striking physiological demonstration of the magnitude of this abnormality in scleroderma.

The ability of the esophagus to empty itself of a 15 ml bolus of 0.1 N HCl is the basis of the acid-clearance test [4, 36]. The finding of abnormal acid-clearing ability in 50 of our patients correlated well with the abnormal peristaltic pattern seen in 51 who had manometry (mild in 10 and moderate to severe in 41). The significance of this finding as a reflection of impaired peristalsis is the demonstration of prolonged contact between refluxed acid and the esophageal mucosa that occurs in most patients with esophageal scleroderma. It is this combination of gastroesophageal reflux and impaired ability of the esophagus to clear the refluxed acid that is responsible for the striking incidence of severe esophagitis and stricture formation in patients with esophageal scleroderma. This incidence was 48% in the series of 26 patients reported by Henderson and Pearson [16] and 25% (13 patients) in our series.

The esophageal acid-perfusion (Bernstein) test [3] is positive in approximately 70% of patients with typical reflux symptoms [36]. A 10-minute intraesophageal acid perfusion, however, failed to produce any symptoms in 37 of our 53 patients with scleroderma. The reason for this is speculative but may be related to the destruction of esophageal sensory pathways that occurs either as smooth muscle atrophy and fibrosis progress or as reflux esophagitis ad-

Fig 6. Normal postoperative acid-reflux test. Note that intraesophageal pH never falls below 4 with a variety of postural maneuvers. (DB = *deep breathing;* V = *Valsalva maneuver;* C = *cough;* HPZ = *high-pressure zone.)*



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vances, with secondary lower esophageal fibrosis.

Having thus established that gastroesophageal reflux, and not just impaired peristalsis, is a major component of esophageal scleroderma and that the combination of these two factors predisposes to the development of severe reflux esophagitis, we think that an aggressive approach to the control of reflux in these patients is indicated if the complications of stricture formation and aspiration are to be avoided (see Fig 4). Strict adherence to a medical antireflux regimen is essential. Esophagoscopy at one- or two-year intervals should be performed to evaluate the presence or extent of esophagitis, irrespective of symptoms. Roentgenographic evidence of distal esophageal stenosis in these patients indicates an advanced stage of reflux esophagitis which could and should have been prevented with earlier detection.

Once mucosal ulceration in esophageal scleroderma is documented by esophagoscopy, we believe that surgical reconstruction of the esophagogastric junction is indicated if the patient's general condition permits it. Lasting control of gastroesophageal reflux with a standard Belsey Mark IV repair, however, is jeopardized by the presence of esophagitis and stricture formation, which prevent a tension-free repair and require that sutures be placed into inflamed distal esophageal musculature and submucosa [9, 27]. In the patient with esophageal scleroderma, the suitability of the distal esophagus for holding sutures is further compromised by the smooth muscle atrophy present. These same considerations also apply to both the Nissen fundoplication and the Hill median arcuate ligament repair, which likewise require sutures in the distal esophagus or periesophageal tissues. Thus, 3 patients in our series who had undergone a total of seven unsuccessful antireflux operations prior to their Collis-Belsey repair had experienced recurrent reflux within weeks to months after each attempt.

The alternative of distal esophagectomy with various combinations of intestinal reconstruction and gastric resection in these patients has been utilized with limited success [6, 30], but the magnitude of these procedures is considerable. Fortunately, as Pearson and associates [31] have demonstrated, salvage of the inflamed distal esophagus is feasible in the majority of cases by combining the esophagus-lengthening gastroplasty technique of Collis and the Belsey procedure with dilation of the esophageal stricture. This has also been our experience, for in the past two years we have operated upon 19 patients with peptic esophageal strictures, in 17 of whom the stricture could be dilated intraoperatively to admit at least a 50F Hurst-Maloney bougie, thus avoiding the need for distal esophagectomy. Collis-Belsey reconstruction of the esophagogastric junction has provided effective control of reflux in 15 of these patients.

Henderson and Pearson [16] reported good to excellent results in 8 of 11 patients with esophageal scleroderma treated in this way. The striking relief of symptoms from reflux obtained in all 11 of our patients, with restoration of a competent distal esophageal valvular mechanism in 7 of 9 patients who have had postoperative acid-reflux testing, adds further support for the combined Collis-Belsey approach in these patients. It is possible that the 2 patients in whom the combined Collis-Belsey repair failed to prevent reflux, despite the roentgenographic demonstration of a 3 to 5 cm length of intraabdominal distal esophagus, had gastric involvement with scleroderma that interfered with compression of the new distal "esophageal" segment by the Belsey fundoplication. This is unlikely, however, since no gross abnormalities of the stomach were seen at operation, and the stomach is least often involved when scleroderma affects the gut. Further, the postoperative distal esophageal HPZ pressures obtained in these patients were comparable to those found after the Collis-Belsey procedure in patients without scleroderma [29].

Theoretically, the combined Collis-Belsey operation in patients with esophageal scleroderma minimizes the risk of recurrent reflux by providing additional healthy, distal "esophagus" around which the two-thirds circumferential fundic wrap can be performed [29]. Tension on the repair is thus avoided, and the need for sutures into inflamed and abnormal esophageal tissues is eliminated.

The major esophageal symptoms of scleroderma are secondary to reflux esophagitis, not impaired motility, and can be effectively controlled by the combined Collis gastroplasty and Belsey Mark IV repair. Systemic disease in these patients is not a contraindication to operation, nor does it preclude normal healing and recovery. However, early recognition of the indications for surgical intervention in patients with scleroderma is critical if maximum benefit is to be derived from the procedure. Undue delay, with subsequent progression of esophagitis, not only diminishes the likelihood of salvaging the esophagus, but also permits cardiac and pulmonary changes to develop that may lead to a prohibitive operative risk.

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Editor's Note

If one of the authors may be permitted to put on another hat, it should be emphasized that the follow-up is short and that additional careful study of these patients is necessary before widespread use of this procedure can be advocated.

Discussion

DR. THOMAS R. DE MEESTER (Palos Heights, IL): I would like to congratulate Dr. Orringer on a superb study in an interesting group of patients and support his findings by presenting a series of studies we did in a patient who had scleroderma, using manometry and 24-hour pH monitoring of the esophagus.

Her motility tracing demonstrated peristalsis in the proximal third of the esophagus, where the striated muscle is present, but complete absence of peristalsis in the distal two-thirds of the esophagus. The area where the distal esophageal sphincter should have been was indicated on manometric tracings only by the respiratory inversion point.

A distal HPZ was obtained following a Belsey antireflux procedure, though a gastroesophageal gradient was still absent. Despite its small size, the HPZ was effective in preventing regurgitation of acid, as was shown by the pH pullthrough study in which the pH changed from 1 in the stomach to above 5 in the esophagus.

Twenty-four-hour pH monitoring tests were done in this patient. Preoperatively the percentage of time the pH in the esophagus was below 4 was abnormally high. However, the number of reflux episodes during the 24-hour period was well within the normal range, normal being 50; the patient had about 30. The average duration of each reflux episode was abnormal. The longest reflux episode preoperatively lasted more than two hours, indicating a large volume of reflux in this patient and difficulty in clearing the reflux contents from the esophagus. Postoperatively the percentage of time the esophageal pH was below 4 was reduced but not down to normal. The number of reflux episodes was also less. However, the antireflux procedure added significantly to the difficulty the esophagus had in clearing refluxed acid. The longest reflux period was reduced but not normal, indicating a diminution in the volume of reflux but continuing difficulty in clearing the esophagus of refluxed contents.

Thus the success of an antireflux procedure in patients with scleroderma depends on reducing the volume of reflux, while at the same time not significantly interfering with the ability of the esophagus to clear itself. To achieve this delicate balance is a difficult thing, and perhaps Dr. Orringer can enlighten us on techniques used in an antireflux repair to achieve this goal.

DR. ROBERT D. HENDERSON (Toronto, Ont, Canada): I think Dr. Orringer's paper is a beautifully developed series and very carefully studied.

In Toronto our experience with gastroplasty and Belsey repair for scleroderma has considerably increased since we first reported our experience, and we continue to be satisfied with the quality of the result achieved. I think it is important to recognize that very satisfactory and often normal swallowing can be restored if effective reflux control is achieved by the operation.

There are two or three points I would like to raise with Dr. Orringer. First, I do not believe that the result achieved with gastroplasty in patients with scleroderma is as good as we see in patients with an otherwise uncomplicated peptic stricture, and I would like to ask if this is his impression as well.

Second, in our particular group, the patients who did best were those with the "CRST" variety of scleroderma (Calcification in the extremities, Raymond's phenomenon, Sclerodactyly, and Telangiectasia), which is a rather slowly developing type compatible with a normal life span rather than the form that may be much more rapid in progression. I think that selecting this particular type of patient is more likely to produce a satisfactory long-term result.

The final point is this. I have been impressed that some patients develop very severe dysphagia postoperatively without a roentgenographically or endoscopically demonstrable stricture and can have complete relief of the dysphagia if one passes a size 60 bougie. I think this is rather critical, in that passing a size 50 bougie in some of the patients I have managed was not nearly as effective. In the adynamic esophagus, when a stricture is present, very slight narrowing in the esophagus will produce major dysphagia, so that dilation to the upper limit of 60F is very important. I would like to ask Dr. Orringer if he has had a similar experience.

DR. ORRINGER: I thank the discussants for their comments. I think Dr. DeMeester's finding of persistent reflux following the Belsey operation for esophagitis in a patient with scleroderma illustrates what we reported in 1970 in a review of the long-term results of the Mark IV repair in nearly 900 patients operated upon in Mr. Belsey's clinic in Bristol, England. A recurrence rate in the range of 45% was found when the procedure was performed in the face of severe reflux esophagitis. I think we all recognize now that any hiatal hernia repair which attempts to pull the esophagogastric junction beneath the diaphragm in the presence of esophageal inflammation and shortening is often destined to fail.

Dr. Henderson's comments are very apropos, and our findings are similar to his. We have demonstrated acid reflux postoperatively, using the intraesophageal pH electrode, in 2 patients whose symptoms of reflux were relieved by operation. Whether this was related to sclerodermal involvement of the stomach, preventing the gastroplasty tube from being compressed as completely as it would be in patients without scleroderma, I don't know. Certainly, when scleroderma affects the gastrointestinal tract, it involves the stomach least often, and I do not think this should dissuade us from using the Collis procedure in this group of patients.

Unquestionably, we are recommending the Collis-Belsey procedure for a patient with the slowly progressing form of scleroderma rather than the rapidly progressing form of the disease, which carries such a terrible prognosis.

We too have noticed dysphagia in a few of these patients without radiographic evidence of stricture or endoscopic evidence of esophagitis. We have attributed this to the impaired esophageal motility in these patients. Almost half of our patients complained of delayed emptying of the esophagus; in 19 it had occurred prior to the onset of any symptoms of gastroesophageal reflux and required them to use large amounts of liquids to wash food down. Unlike Dr. Henderson, we have not treated such patients with esophageal dilations.

In closing, I wish to reemphasize our belief that the Collis-Belsey procedure for esophageal scleroderma should be performed relatively soon after ulcerative esophagitis has been established endoscopically. If one delays treatment of the reflux esophagitis in these patients, the progressive pulmonary and cardiac changes of scleroderma may be responsible for a prohibitive operative risk once the decision for more aggressive therapy is made.

Interruption of Patent Ductus Arteriosus in Premature Infants with Respiratory Distress Syndrome

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Alois R. Hastreiter, M.D., Edward J. Bennett, M.D.,
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ABSTRACT **In infants with respiratory distress syndrome (RDS) hypoxemia inhibits closure of the patent ductus arteriosus (PDA), resulting in increased pulmonary blood flow with subsequent increased hypoxemia. In an attempt to interrupt this cycle 42 consecutive premature infants with RDS and PDA, weighing between 550 and 2,000 gm (average, 1,383 gm) and with an average gestational age of 31 weeks, were arbitrarily treated either medically (13 patients) or by interruption of the PDA (20 patients). Eleven patients who were initially treated medically could not be weaned from the respirator and later underwent operation. There were no operative or anesthetic deaths; late survival was 65% (20 patients).**

The last 31 patients were randomly divided into operative and nonoperative groups. Preliminary results revealed no significant differences in late survival between the two groups. Since the operative risk is minimal, further investigative efforts are indicated to settle this issue.

The combination of prematurity, respiratory distress syndrome (RDS), and the presence of a patent ductus arteriosus (PDA) is frequently found in neonatal distress. In addition, hypoxemia inhibits closure of the PDA in premature infants with RDS, causing an increase in pulmonary blood flow, which—assuming the presence of a left-to-right shunt—results in further hypoxemia. If this state is allowed to progress, congestive heart failure may ensue, resulting in further deterioration of pulmonary function and continuation of this vicious cycle leading to death.

Several conflicting reports have appeared in the literature indicating the salutary effects of PDA interruption to treat this spectrum of events [9, 10, 17, 21, 23, 27]. However, most of the studies either have involved too few patients or have examined mixed groups of patients operated upon for congestive heart failure following unsuccessful pharmacological therapy. There have been no previous studies limited to the relationship of PDA and RDS before the onset of congestive heart failure, nor have any randomized controlled studies been reported. The purpose of this article is to present our entire medical and surgical experience in 42 consecutive premature infants with severe RDS and PDA in an attempt to determine whether early operative intervention will decrease the morbidity and mortality of RDS. The last 31 patients in this series were treated as part of a prospective randomized study, and this report analyzes our preliminary findings.

Methods

Patient Selection

All the patients were admitted to the high-risk nursery at the University of Illinois Medical Center between August 4, 1973, and December 8, 1975; two-thirds of the patients had been transferred from other institutions. The 42 patients in this series were divided into two groups: Group 1, consisting of 11 infants of whom 10 were arbitrarily subjected to operative intervention because of deterioration following standard medical treatment, and Group 2, 31 patients who were randomly divided into either surgical or medical categories and are part of an ongoing clinical study (Table). Since the results achieved in Group 1 patients suggested that surgical intervention involves minimal risk, the Clinical Research Review Board at our institution suggested that patients admitted to the study and assigned to medical therapy should

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Clinical Data and Results in 42 Infants Having PDA Interruption for RDS

No. of Patients	Treatment	Birth Weight (gm)	Gestational Age (wk)	Respirator Support (days)	Survival		Survival Age (days) when:		
					Number	%	PDA Detected	Extubated	Discharged
Group 1									
10	Surgical	1,259 ± 396	31 ± 2	27.2 ± 12	3	30	4.3 ± 2	...	84.3 ± 8
1	Medical	1,850	32	9	1	100	9	...	27
Group 2									
8	Surgical	1,421 ± 460	31 ± 5	27.2 ± 12	4	50	6 ± 1	22.5 ± 2[a]	90.5 ± 27
12	Medical	1,476 ± 422	32 ± 3	10 ± 6	7	58	4.3 ± 1	10.4 ± 5[a]	191.3 ± 27
11	Medical failure, operation	1,397 ± 463	30 ± 3	31.9 ± 20	9	82[a]	5.9 ± 2	31.3 ± 13[a]	204 ± 26

[a] $p < 0.05$.

undergo operation if, after ten days, medical treatment was unsuccessful. Thus there were three subgroups: surgical, medical, and medical failures who subsequently underwent operation (Fig 1). Before a patient was entered into the Group 2 study, informed consent was obtained from the parents.

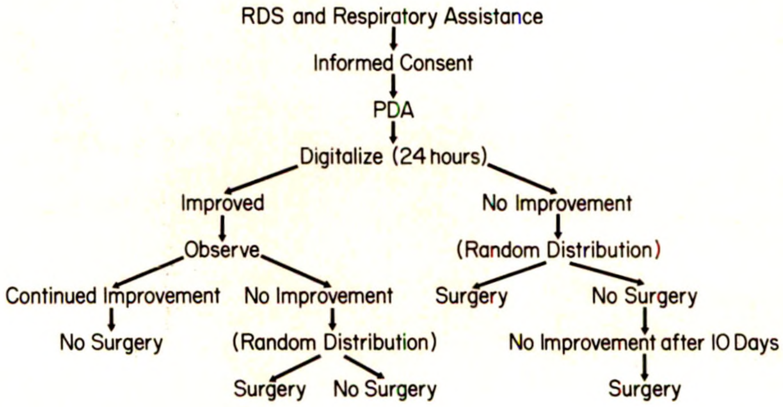
Diagnosis of RDS

The clinical features of RDS have been clearly defined by Silverman [26], Downes [8], and their co-workers. The most significant feature of the disease is the infant's inability to maintain adequate oxygenation while breathing room air. Although there may be many other causes of respiratory distress such as congenital anomalies, upper airway obstruction, congenital heart disease, infections, and aspiration, the most common form of respiratory distress in the newborn is hyaline membrane disease.

The diagnostic criteria for RDS in this study were:

1. Onset of respiratory distress within 6 hours following birth and persisting for more than 4 hours.
2. Prematurity, defined as a gestational age of less than 37 weeks.
3. Presence of historical risk factors such as cesarean section delivery or a diabetic mother.
4. Abnormal chest roentgenograms, consisting of a diffuse reticulogranular pattern associated with poor aeration of the lung parenchyma.
5. Abnormal arterial blood gases, with the Pa_{CO_2} greater than 60 torr and Pa_{O_2} below 40 torr when breathing room air.
6. Need for nasotracheal intubation and mechanical respiratory assistance.

Fig 1. Protocol for prospective randomized study of RDS and PDA.



Diagnosis of PDA

All the infants admitted to the hospital with a diagnosis of RDS were evaluated daily for clinical signs of a PDA. A diagnosis of PDA was made if two or more of the following findings were present:

1. Hyperactive precordium.
2. Bounding peripheral pulses.
3. Heart murmur at the upper left sternal border.
4. Third heart sound or middiastolic rumble at the apex.

Hepatomegaly and a typical continuous murmur were present in some patients.

After the diagnosis of PDA was made, the infants were digitalized. Patients weighing less than 1,000 gm received 20 μg/kg of digoxin; those over 1,000 gm were given 40 μg/kg. Diuretics were added as required. Blood transfusions were given when necessary to keep the hematocrit above 40%. Within 24 hours after digitalization was begun, the infants were reevaluated for evidence of improvement in respiratory status as judged by improvement in blood gases, decrease in inspiratory oxygen concentration, or change to a lesser degree or type of respiratory assistance. Infants who showed improvement continued to receive digoxin and were observed; they form part of the medically treated group. Those who did not improve or whose condition deteriorated after initial improvement were subjected to random treatment selection (see Fig 1).

Treatment of RDS

The basic principles of management for infants with hyaline membrane disease are based on providing an adequate thermal environment and sufficient calories, treating acidosis, correcting hypovolemia, and ensuring adequate oxygenation through respiratory support [14, 27, 29]. The respiratory and circulatory status were evaluated every 24 hours by two pediatricians, a neonatologist and a cardiologist. If surgical therapy was selected, the operative procedure was performed within 12 to 24 hours.

Operation

All infants were transported to the operating room in a warmed incubator by an anesthesiologist. The basic anesthetic agent was 50% nitrous oxide in oxygen with controlled rebreathing utilizing a Rees variation of the Ayre's T-tube, so that the Pa_{CO_2} was limited to a range of 35 to 40 torr. This was achieved by limiting the fresh gas flow from the anesthesia machine, and the type of ventilation was that achieved with a T-piece, at a low volume and rapid rate and with a moderate amount of positive end-expiratory pressure [4]. The ancillary agent was tubocurarine or pancuronium at doses of 250 and 30 μg/kg, respectively [5]. Because of the obviously limited surface area, the neonate was not placed on a warm-water mattress, but rather the operating room temperature was raised to 32°C.

During the procedure the temporal pulse, temperature, and electrocardiogram were monitored. Blood pressure, blood gases, and other indicators, though helpful, were used only if available and easy to obtain. The intravenous fluid administered, 5% dextrose in lactated Ringer's solution, was limited to the amount required to ensure that drugs given through the intravenous tubing would reach the patient, and it was not allowed to exceed 3 ml/kg/hour [3]. An oral endotracheal tube was used during the operation and was replaced at the end of the procedure by a nasotracheal tube, which was checked for position and length by a chest roentgenogram when the patient was returned to the high-risk nursery.

The ductus arteriosus was exposed through a posterolateral thoracotomy in the fourth intercostal space [12]. On observation, the ductus varied from two-thirds to one and one-third the size of the aorta. In several instances the ductus was noted to constrict during the dissection. The ductus arteriosus was singly or doubly ligated, depending on its length, with 1-gauge silk. There were no untoward events during any of the operations that necessitated administration of blood or inotropic agents, nor did we observe the increased friability of the ductus noted by previous authors [9]. Open thoracotomy was limited to 15 minutes. There were no anesthetic or early postoperative deaths.

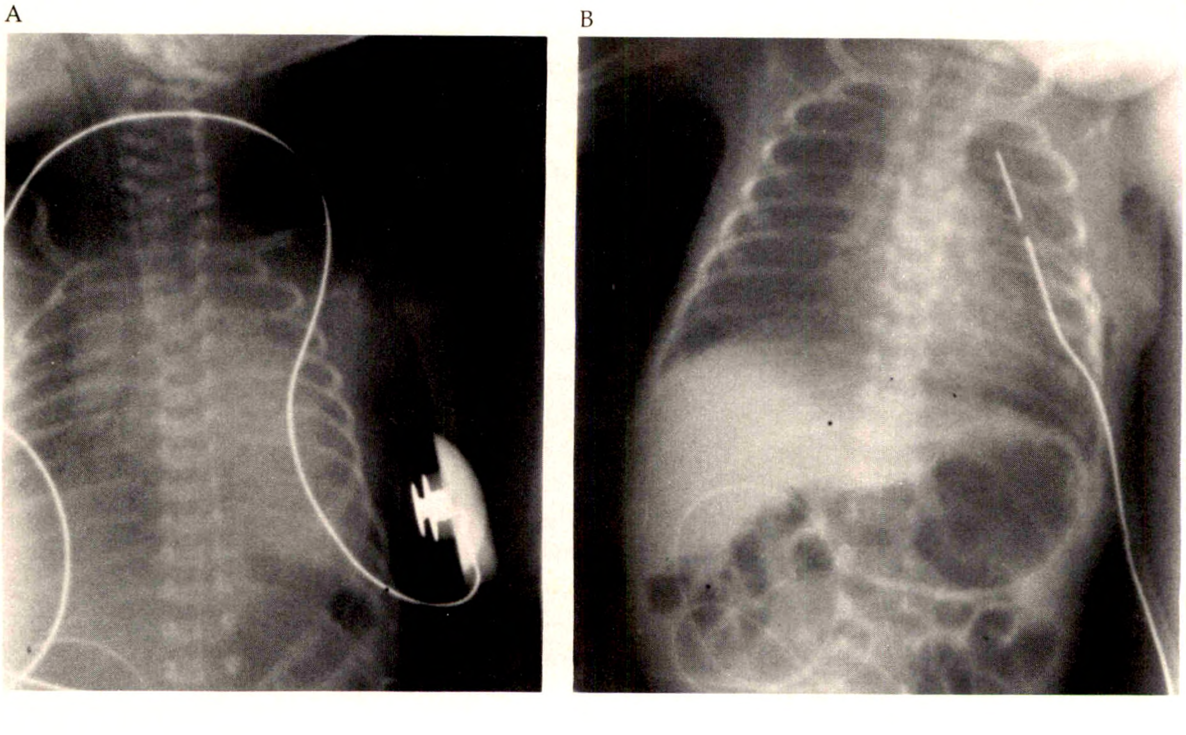
Results

Clinical data for the 42 infants studied in the entire series are summarized in the Table. There were no significant differences between subgroups with respect to birth weight, gestational age, and age at PDA detection. Similarly, there were no differences in total time of mechanical ventilation except for the medically treated patients in Group 2. These latter differences are to be expected in view of the fact that ventilated infants in this group who were not improving after ten days of medical therapy were shifted, by virtue of the protocol, to the surgical group (ie, medical failure and operation).

In order to compare the effectiveness of each of the treatment modalities, success was measured in terms of survival at discharge. When viewed in their totality (Groups 1 and 2) there were no significant differences between the medically treated and operated groups—62% versus 55% survival, respectively. Nevertheless, when late operative survival was achieved, the change in clinical condition with rapid clearing of pulmonary congestion was often dramatic (Fig 2). There were no differences in survival between the medical and surgical subgroups of the randomized study (Group 2), with 58 and 50% survival, respectively. However, there was a significantly increased survival of 82% in the medical failure–surgical subgroup ($p < 0.05$). These differences were anticipated, since this subgroup was preselected and admittance to it required at least ten days' survival. As would be expected, the ten days of mechanical ventilation for the medical failure–surgical group delayed extubation significantly compared with the surgical group ($p < 0.05$) (see the Table). The greatest salutary effect of early operative intervention appeared to be early discharge, in that patients in the surgical subgroup were discharged at 90.5 ± 27 days of age compared with 191.3 ± 27 and 204 ± 26 days, respectively, in the medical and the medical failure–surgery subgroups.

Since the number of patients in each of the subgroups is small, these differences must be viewed only as preliminary findings until the total study, numbering in excess of 75 patients, is completed.

Fig 2. Chest roentgenograms obtained from a patient in Group 1. (A) Preoperative roentgenogram shows diffuse reticulogranular pattern of the lung parenchyma, with cardiac enlargement. (B) Roentgenogram obtained 4 hours postoperatively reveals marked clearing of the lung fields and a decrease in cardiac size.



Comment

There is ample evidence to show that the incidence of PDA is higher in premature as compared with term infants and is even higher in premature infants with RDS [7, 11]. The mechanisms for persistence of the PDA are thought to relate to the reduced cholinergic innervation of the ductus and the decreased ductal response to oxygen, resulting in a loss of vasoconstrictive ability [1, 20].

The rationale for interruption of the PDA in infants with RDS is based on the assumption that a left-to-right shunt is present and significantly increases pulmonary blood flow. Thus, the relationship of pulmonary vascular resistance (PVR) to systemic vascular resistance is of paramount importance. Since the ratio of pulmonary arterial muscular tissue to lung parenchyma is low in the 21-week-old fetus and gradually increases with age, the PVR will be lower in the premature than in the term infant [29]. However, acidosis, hypercapnia, hypoxemia, and positive-pressure ventilation tend to raise PVR [19, 21]. It has been shown that increased pulmonary blood flow without heart failure has a negligible effect on gas exchange and that substantial intrapulmonary shunting with transudation of fluid does not occur until there is left atrial pressure and volume overload [17, 18]. On the other hand, lung compliance declines with small increases in pulmonary blood flow [15]. Hence, several observers have thought that PDA interruption is not indicated unless congestive heart failure is present or a significant left-to-right shunt is demonstrated by aortography [9, 27]. Others, however, have suggested that prompt PDA ligation may prevent the development of severe bronchopulmonary dysplasia [10, 22].

It is obvious from all the conflicting data that a prospective randomized study of the various therapeutic options is necessary. Before embarking on a study of this type, in which there may be small differences, it is obvious that surgical morbidity and mortality must be negligible. Our data, as well as those of others, indicate that this is the case [10, 16]. In addition, survival following medical therapy in an institution undertaking this study should be comparable to that observed in other institutions. Neal and associates [21] have described 396 infants with RDS admitted from January, 1970, to December, 1972, with a 29% survival in patients who had assisted ventilation, which is comparable to the 58% survival in our medical subgroup.

The classic signs and symptoms of PDA are frequently lacking in infants, and in premature neonates with RDS the signs may be evanescent and altered by pulmonary disease and assisted ventilation [2, 23]. In addition, recurrent bradycardia and apnea, tachypnea, pulmonary rales, rising Pco_2, increasing opacification of the lungs, and decreasing respiratory function after initial improvement have been found to be signs of a PDA complicating RDS. Like others [2, 9], we found that the electrocardiogram does not have great diagnostic value, though it may serve to exclude associated congenital heart defects. Similarly, the chest roentgenogram is of little diagnostic value during the acute phase of RDS, as the cardiac and pulmonary vascular shadows are obscured by opacification of the lungs.

Although the signs are atypical, a clinical diagnosis of the presence of a PDA can usually be made. Evaluation of the magnitude of the left-to-right shunt is more difficult. Cardiac catheterization, advocated by some authors, carries significant risk in a sick premature infant and yields little more useful information than an aortogram obtained through an umbilical artery catheter [9, 16, 27]. However, shunt size can be evaluated by an even safer, noninvasive technique—echocardiography. Carter and Bowman [6] have shown echocardiographic left atrial dimension to correlate well with the magnitude of left-to-right shunts in patients with ventricular septal defect. The same principle has been applied to infants with RDS and PDA. Investigators have used increases in the left atrial/aortic root ratio to identify premature infants with RDS who had a large left-to-right shunt [24]. Goldberg and colleagues [13], in a preliminary report of a prospective study using echocardiographic criteria, indicated that the ratio was helpful in selecting 13 out of 83 premature infants with RDS and PDA for operative intervention.

This preliminary report of a prospective, randomized study evaluating the effects of PDA in premature infants with RDS suggests no evidence of increased survival with early operative interruption of the PDA. Since the operative procedure appears to carry minimal risk, further investigative efforts are indicated and necessary to settle this issue.

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Discussion

DR. GERARD A. KAISER (Miami, FL): I congratulate Dr. Levitsky and his associates on this very fine paper and commend them for the use of a randomization protocol in this study.

We have recently reviewed a similar group of 2 infants operated upon between May, 1972, and July,

1975. Our results support their views, first, that no formal cardiac catheterization is required for physical diagnosis and that noninvasive techniques will establish the diagnosis, and second, that within the proper setting an operation can be performed with minimal operative mortality. We too have been fortunate in having no operative deaths in this group of patients.

I do believe, however, that there are two groups of patients who fall into this general category. Eleven of the 20 infants we operated upon had severe associated hyaline membrane disease that necessitated mechanical ventilatory support from the first day of life. Only 3 of these infants ultimately survived to leave the hospital; the others died from various associated anomalies as well as their severe pulmonary disease. In contrast, 8 of the 9 infants in the other subgroup, with severe congestive heart failure and RDS but without hyaline membrane disease, are alive even though these infants required ventilatory support prior to operation.

I think surgical ligation of the PDA in a premature infant is an appropriate and successful mode of therapy when congestive heart failure is refractory to medical management. Proof is lacking, however—as Dr. Levitsky states—to establish its efficacy in the management of premature infants with hyaline membrane disease. I look forward to future reports from his group on the randomized study of this subset.

DR. ROSS KYGER (Houston, TX): I would also like to congratulate Dr. Levitsky and his colleagues on a very well done study. At the Texas Heart Institute and Texas Children's Hospital, we too have struggled with the dilemma of when to operate on these tiny infants with a patent ductus. As experience has accumulated, our neonatologists have tended to favor earlier surgical therapy. They now believe that any premature infant with a ductus who requires five days of mechanical ventilatory support is a candidate for ligation.

The echocardiogram has proved to be a very useful tool in helping us differentiate the relative contribution of congestive heart failure and hyaline membrane disease to the infant's pulmonary problem. With the echocardiogram one can determine left atrial size and compare it to the size of the aortic root. By following this ratio, one can then gauge the effectiveness of medical therapy for congestive heart failure. If the left atrium should enlarge despite adequate medical therapy, the child then has the ductus ligated. We use an extrapleural approach and perform the procedure with the infant in an Ohio warmer in order to maintain the body temperature.

We have operated on 35 such infants, with 30 survivors leaving the hospital. Our neonatologists assure us that modern ventilatory methods are preserving the essential nervous system function of these babies, but they think prolonged respiratory support contributes to the problem of pulmonary dysplasia. Since the procedure has proved to be safe even in infants weighing less than 1,000 gm, we think it should be used early in an effort to shorten respirator time and preserve pulmonary function.

DR. LEVITSKY: I thank the discussants for their kind supporting remarks.

I want to be certain that we have differentiated the types of patients we operated upon, because the literature is quite obscure on this point. The indication for operation in this group of patients is *not* congestive heart failure secondary to a large PDA with a huge left-to-right shunt; in fact, we have not measured the shunt size in our patients. Our indication for operation in this study was hyaline membrane disease plus the presence of a PDA. It has been shown, as we indicated in the paper, that even patients with a small shunt that is not necessarily large enough to increase the size of the left atrium will exhibit a decrease in pulmonary compliance.

In conclusion, I wish to emphasize that the group of patients we have reported is a small subgroup of all the infants with respiratory distress syndrome.

Patent Ductus Arteriosus Ligation and Respiratory Distress Syndrome in Premature Infants

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Gary L. Way, M.D., and James R. Stewart, B.A.

ABSTRACT **Ligation of a patent ductus arteriosus was carried out in 22 premature infants, 20 with concomitant respiratory distress. The duration of high-volume shunting is critical in determining the prognosis for these infants. Because of the low surgical mortality and morbidity and the high incidence of bronchopulmonary dysplasia in babies managed conservatively, infants with respiratory distress syndrome (RDS) who are respirator dependent should undergo ligation as soon as the presence of large left-to-right shunting is determined. Premature infants without RDS or those with mild RDS who are not respirator dependent can be managed medically or with elective ligation. Surgical intervention is strongly indicated in patients with persistent congestive heart failure and respiratory failure. Echocardiography offers an accurate and risk-free approach to the early diagnosis of a large left-to-right shunt through the ductus.**

Delayed spontaneous closure of the ductus arteriosus is common in premature infants. In infants without complicating respiratory problems or with mild respiratory distress syndrome (RDS) not requiring respirator support or positive-pressure ventilation, left-to-right shunting may persist for long periods with few deleterious effects. Among infants with severe RDS, however, mortality and morbidity rates are high, largely due to delayed pulmonary complications (ie, bronchopulmonary dysplasia). If the ductus arteriosus remains patent, or becomes patent, during an early hypoxic episode, respirator support may have to be continued long after primary pulmonary disease has cleared. In this situation the incidence of pulmonary complications due to prolongation of respirator support increases.

Gay and co-workers [4] have defined large shunt duration (LSD) as the period from the onset of large-volume shunting (OLS) to the day of operation. Examination of our own patients and the relevant literature further establishes the value and significance of the LSD. The OLS has been defined clinically as the appearance of a typical murmur, bounding pulses, increased heart size, and greater pulmonary vascularity. Clinical criteria are unreliable as indicators of the presence of a large left-to-right shunt through a patent ductus arteriosus (PDA). The echocardiogram may offer a safe and effective method for confirming the magnitude of the shunt and early determination of the OLS.

Material and Methods

Twenty-two premature infants underwent extrapleural ligation of a PDA at the University of Colorado Medical Center between September, 1972, and July, 1975. Birth weights ranged from 830 to 2,780 gm, and at the time of operation they varied from 760 to 3,420 gm (Table 1). All patients were operated upon through a left extrapleural posterolateral thoracotomy. In a few patients minimal tears were made in the pleura, but in no case was a chest tube left in place at the end of operation. The extrapleural approach was used to minimize handling of the lung and to avoid postoperative chest tube drainage. The average duration of operation was about 25 minutes. Blood loss was negligible, and transfusion was never required.

Twenty infants developed RDS of varying severity early in life. When respiratory failure occurred, continuous positive airway pressure (CPAP) or mechanical ventilation was used. All 20 infants were mechanically ventilated prior to

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Table 1. Characteristics of the Study Population

Patient No.	Birth Weight (gm)	OLS (days)	LSD (days)	Weight at Operation (gm)	Age at Operation (days)	Result
1	1,700	11	3	1,320	14	Lived
2	1,030	6	18	900	24	Died
3	1,100	2	9	900	11	Died
4[a]	1,540	6	22	1,380	28	Died
5	2,780	3 wk	12 wk	3,420	87	Lived
6	940	5	30	1,073	35	Lived
7	830	7	18	760	25	Died
8	1,360	8	7	1,000	16	Lived
9	940	8	6	770	14	Lived
10	1,520	4	6	1,320	10	Lived
11	1,100	5	55	1,160	60	Lived
12	1,000	20	55	2,140	75	Lived
13	1,380	9	13	1,240	22	Lived
14[a]	1,120	14	12	1,180	26	Lived
15	n/a	16	30	n/a	46	Died
16	n/a	Birth	18	n/a	18	Died
17	n/a	7	5	n/a	12	Lived
18	n/a	7	8	n/a	15	Lived
19	960	4	4	800	8	Lived
20	1,077	23	5	1,200	28	Lived
21	1,800	3	8	1,500	11	Lived
22	1,000	11	1	880	12	Lived

[a]Twins.
OLS = Onset of large-volume shunting; LSD = large shunt duration.

operation. The patients were divided into groups according to the severity of their RDS: infants without RDS (2 patients), infants with mild RDS who were not respirator dependent (6 patients), and infants with severe RDS who required either respirator assistance or CPAP (14 patients). In all cases the OLS was determined clinically as the onset of a typical murmur, bounding pulses, cardiomegaly, increased pulmonary vascularity, and rising Pa_{CO_2}. The LSD was the interval between OLS and time of operation.

Silverman and associates [15] first described the usefulness of the ratio between left atrial and aortic root diameters, as measured echocardiographically, in determining the magnitude of left-to-right shunting through a ductus. Echocardiograms were made in 11 of the 22 infants reported here, and the left atrial/aortic root ratios were calculated. A ratio greater than 1.0 was taken as evidence of left-to-right shunting. Whenever possible, serial readings were made preoperatively, as persistently large or increasing ratios are more important than single estimations (Fig 1).

Results

The postoperative mortality rate (death during same hospital stay) was 22.7%, 5 of the 22 infants. All patients who died had had RDS and were respirator dependent. One patient (No. 3) died 5 days after going home; this was 95 days after operation and 106 days after birth. The 5 deaths in the hospital occurred 4, 5, 6, 16, and 67 days after operation, respectively; the causes of death are listed in Table 2. No infant died as a direct result of the operative procedure. Even early postoperative deaths were due to other causes such as necrotizing enterocolitis, contralateral respirator-induced pneumothorax, and central nervous system hemorrhage.

Atelectasis and pneumothorax were observed

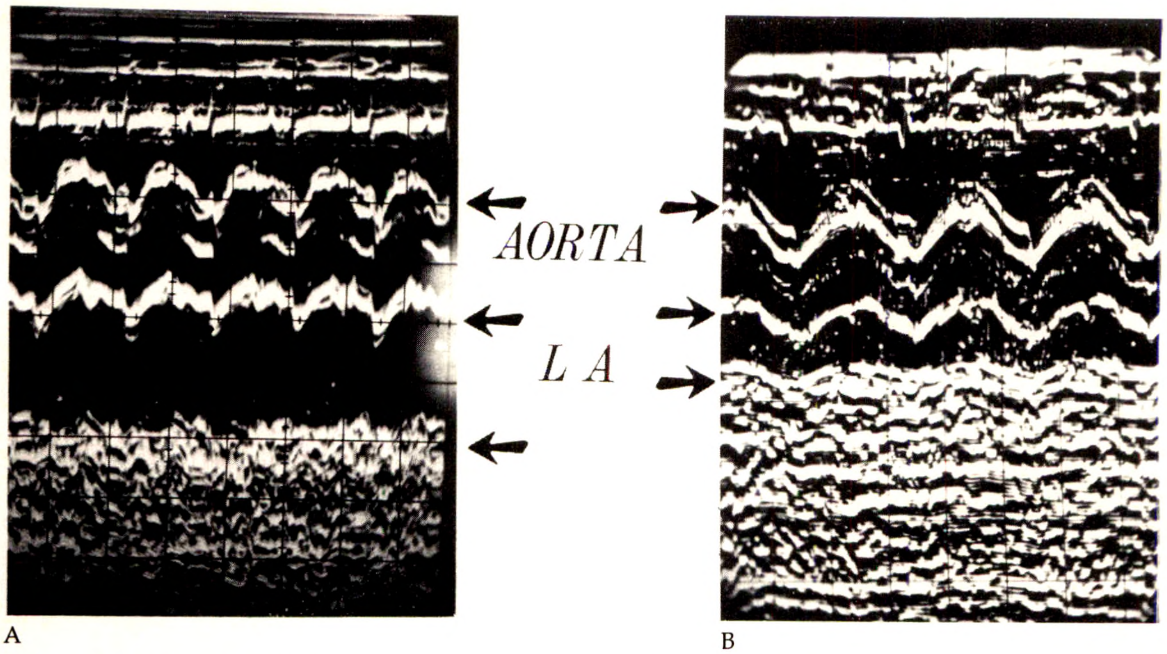

Fig 1. (A) Preoperative and (B) postoperative echocardiograms showing reduction in left atrial/aortic ratio. The postoperative echocardiogram was made 24 hours after operation. (LA = *left atrium.)*

both preoperatively and postoperatively but could not be attributed to the surgical procedure. Chronic respiratory disease persisted in 1 patient for two years postoperatively. The child was readmitted three times for pneumonia, asthma, and bronchitis. This complication was probably a result of prolonged respirator dependence. No instances of recurrent laryngeal neuropathy, pulmonary artery laceration, or other specifically surgical complications were observed.*

The OLS in the 5 infants who died in the hospital occurred at a mean age of 7.0 days. The mean LSD for these patients was 21.2 days (±5.7) and ranged from 18 to 30 days (Table 3). In infants who survived but who developed respirator-dependent RDS, the average OLS was 7.0 days. The mean LSD for these infants was 5.0 days (±2.3). The LSD for infants with severe RDS who survived was never longer than that for similar infants who died. No deaths occurred among infants with mild RDS or without RDS, even though the LSD in these groups averaged 20.6 (±19.0) and 69.5 days (±14.5), respectively.

For infants with respirator-dependent RDS, the mortality rate associated with an LSD of 8 days or less was 0. The mortality rate accompanying an LSD greater than 8 days was 100%.

Eleven infants underwent echocardiography

Table 2. Causes of the Hospital Deaths

Patient No.	Age at death (days)	Days Postop	Cause of Death
2	30	16	BPD, RDS, left pneumothorax, CNS hemorrhage
4	95	67	BPD, O_2 toxicity
7	30	5	NEC, renal failure
15	50	4	Right pneumothorax
16	24	6	Unknown

BPD = bronchopulmonary dysplasia; RDS = respiratory distress syndrome; NEC = necrotizing enterocolitis.

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*Average FI_{O_2} concentrations in patients who survived without bronchopulmonary dysplasia (BPD) were: 37% before operation, 47% the day after operation, 27% one week later. In infants who developed BPD, preoperative FI_{O_2} concentrations were greater than 80% and remained so postoperatively.

Table 3. Large Shunt Duration and Mortality Data in the 22 Infants

No RDS (N = 2)	Mild RDS (N = 6)	Severe RDS (N = 14)	
LSD in Survivors (days)	LSD in Survivors (days)	LSD in Survivors (days)	LSD in Nonsurvivors (days)
84	30	3	18
55	55	7	9
	13	6	22
	12	6	18
	8	5	30
	5	4	18
		8	
		1	
$\overline{69.5}$	$\overline{20.6}$	$\overline{5.0}$	$\overline{19.1}$ (21.2[a]; n = 5)

[a]Mean value for hospital mortality.
LSD = large shunt duration.

preoperatively. Accurate information was available for 10 of the 11 infants. The left atrial/aortic root ratios varied between 1.0 and 1.83 (Table 4).

Comment

There is a very high incidence of patency of the ductus arteriosus after birth in premature infants. Rudolph [14] reported that nearly two-thirds of all infants with a birth weight less than 1,750 gm have clinical evidence of a patent ductus, and in infants weighing less than 1,000 gm at birth the ductus is almost invariably patent. In a large percentage of premature infants, hyaline membrane disease is also present. Although there does not appear to be a direct causal relationship between patency of the ductus and RDS, both problems are related to prematurity. The high incidence of PDA in premature infants is probably due to both a high threshold of response of the immature ductus to oxygen and contractile inadequacy of the immature ductal musculature.

An explanation for the apparently increasing clinical experience with PDA is that more preterm infants with RDS are surviving than was the case a few years ago. Paradoxically, the maintenance of $\mathrm{Pa_{O_2}}$ below 100 mm Hg to avoid retrolental fibroplasia may further contribute to the high incidence of PDA. Presently, every effort is made to prevent the $\mathrm{Pa_{O_2}}$ from rising above 70 to 80 mm Hg, a level that is not adequate to stimulate ductal constriction in premature infants. The successful treatment of RDS and prevention of retrolental fibroplasia may therefore combine to increase the incidence of PDA in these infants [14].

Early ligation of the PDA may or may not be indicated in preterm infants. Patent ductus ligation has been reported in 178 premature infants in the literature [5, 6, 12]. Although increasing numbers of infants have undergone ligation with varying results, the criteria for advocating operation are currently vague.

Kilman and colleagues [8] believe that $\mathrm{Pa_{CO_2}}$ is probably the most sensitive indicator of patient progress. If the $\mathrm{Pa_{CO_2}}$ increases in spite of ventilator support, the ductus should probably be ligated. Thibeault and co-workers [16] use the criteria of the need for increasing the inspired oxygen fraction and peak inspiratory pressure as well as heart size as indicators for surgical intervention. They also confirm the presence of left-to-right shunting through the ductus by retrograde aortography and determine the magnitude of shunting by the rate of disappearance of contrast medium from the aortic arch into the pulmonary artery. Coran and associates [3] use a figure of 50% shunt by indicator-dilution as a criterion for operation.

These phenomena used to evaluate patient progress are consequences of a large left-to-right shunt. A more desirable approach would be to

Table 4. Echocardiographic Findings in 10 Infants

Patient No.	LA/AO	Ductus Size (mm)	Interval from OLS to EC (days)	Interval from US to OP (days)
1	1.83	4	1	2
3[a]	1.2–1.5		0	18
14[b]	1.1	Large	6	6
4[a,b]	1.2	Large	14	8
7[a]	1.3	Large	8	10
11	1.2	4	6	49
19	1.0	4	−3	7
	1.2		OLS	4
	1.6		4	0
20	1.5	3	0	5
	1.4		3	2
	1.3–1.4		4	1
	1.3		5	0
21	1.3–1.6	6	1	4
	1.6		2	3
22	1.2	4	−9	10
	1.2		−6	7
	1.35		0	1

[a] Died.

[b] Twins.

LA/AO = left atrium/aorta ratio. OLS = onset of large shunting; EC = time of echocardiography; US = ultrasonography; OP = time of operation.

attempt early detection of shunting by noninvasive means and to use this information, as well as the knowledge of the complications that may arise due to its presence, as criteria for advocating operation.

Gay and colleagues [4] reported 45 patients in whom the LSD was used as an indication for operation; it could also be correlated with the later development of bronchopulmonary dysplasia and was therefore of prognostic value. The LSD in their patients with severe RDS was 1.5 days in survivors and 4.1 days in nonsurvivors. The LSD in our patients with RDS who survived averaged 5.0 days, which suggests that the patients reported by Gay's group were operated on sooner than were ours.

If the LSD criteria are applied to other reported series (Table 5), the LSD for patients with severe RDS who survived was significantly shorter than for those who died ($p < 0.015$). Of 91 patients with RDS, 57 lived and 33 died. Those who survived had a mean LSD of 7.7 days (±9.2), whereas the LSD for those who did not live averaged 10.9 days (±11.1) ($p < 0.10$). In these series, 61 patients had severe RDS; 31 lived and 30 died. The average LSD for the survivors was 3.9 days (±7.0), compared with 9.0 days (±8.8) for those who died. The average LSD among 26 surviving infants with mild RDS was 12.3 days (±11.5); the average LSD among the 4 infants with mild RDS who died was 25.5 days (±17.1) ($p < 0.30$). These figures support the concept that the duration of the large shunt is critical in determining the mortality rate for infants with respirator-dependent RDS and PDA (Fig 2). Current information indicates that for patients with RDS and a PDA who are respirator dependent, the shorter the LSD, the lower the mortality rate (Table 6). Among reported patients there has been only 1 survivor in this group in whom the LSD was greater than 8 days. In severe RDS, the mortality rate has been 92% in patients with an LSD greater than 8 days but only 37.5% when the LSD was less than 8 days.

The mortality rate in infants who underwent PDA ligation is summarized in Table 7. The

Table 5. Large Shunt Duration and Reported Success in the Literature

	No RDS				Mild RDS				Severe RDS			
Author	LSD (days)	L	LSD (days)	D	LSD (days)	L	LSD (days)	D	LSD (days)	L	LSD (days)	D
Clarke[a]	69.5	n = 2	. . .	. . .	20.6	n = 6	. . .	. . .	5.0	n = 8	21.2	n = 5
Horsley[a]	. . .	. . .	. . .	. . .	14	n = 5	42	n = 1	. . .	. . .	11	n = 3
Gay[a]	5.2	n = 11	1	1	8.6	n = 3	. . .	. . .	1.5	n = 16	4.1	n = 14
Murray[a]	80	n = 2	. . .	. . .	10.6	n = 3	28	n = 2	3.5	n = 2	8.6	n = 3
Neal[a]	. . .	. . .	. . .	. . .	21	n = 1	. . .	. . .	20.5	n = 2	2.5	n = 2
Lewis[a]	. . .	. . .	. . .	. . .	3.2	n = 5	4	n = 1	3	n = 3	6	n = 1
Kitterman	22	n = 4	. . .	. . .	14	n = 2	. . .	. . .	24	n = 1	24	n = 2
Gupta[a]	. . .	. . .	. . .	. . .	10.7	n = 3	. . .	. . .	. . .	. . .	28	n = 1
Thibeault	. . .	. . .	. . .	. . .	5	n = 8	5	n = 6	5.6	n = 5	5.6	n = 2

[a]Used to calculate values quoted in text.

RDS = respiratory distress syndrome; LSD = large shunt duration; L = lived; D = died.

range is from 50% [11] to 20% [9, 10]. The mean mortality was 30%. Duration of medical therapy varied from 1 day to 3 weeks. None of the deaths were directly related to operation, and only 2 occurred within 24 hours of the procedure. Most deaths were due to progressive respiratory failure 1 week to 8 months following operation. Other deaths were caused by necrotizing enterocolitis, central nervous system hemorrhage, and meningitis. Most infants who died had bronchopulmonary dysplasia at the time of their demise, regardless of the cause of death.

Mortality rates, however, do not tell the entire story. There are patients who survive but remain respiratory cripples because of bronchopulmonary dysplasia. One infant in our

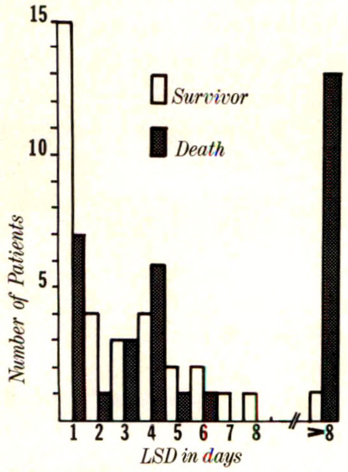

Fig 2. Survival and death at different shunt durations among patients with severe respiratory distress syndrome. (LSD = *large shunt duration.)*

Table 6. Large Shunt Duration and Hospital Mortality after PDA Ligation in Premature Infants with RDS

	Mortality (%)	
Condition	LSD < 8 Days	LSD > 8 Days
Severe RDS with PDA	37.5	92
Mild RDS with PDA	8.3	17.6

Table 7. Hospital Mortality after PDA Ligation in Premature Infants

		Deaths	
Author	No. of Patients	Number	%
Kilman	12	3	25
Horsley	9	4	44
Murphy	10	5	50
Gupta	4	1	25
Kitterman	10	2	20
Gay	45	15	33
Lewis	10	2	20
Neal	5	2	40
Thibeault	21	8	38
Coran	30	7	23
Clarke	22	5	23
Total	178	54	30

series, followed for two years, had numerous admissions related to bronchitis, pneumonia, and asthma. Thus, there may be chronic morbidity primarily due to prolonged respirator support during early infancy.

In all series the OLS was determined from the clinical criteria presented in the respective study. If detailed information as described earlier was not available, relevant information from the report (eg, onset of murmur, congestive heart failure, or cardiomegaly) was used to estimate the OLS. The LSD was determined in the usual manner.

Echocardiographic measurement of the left atrial/aortic ratio can be used to detect a significant left-to-right shunt prior to onset of many of the typical physical findings. In 1974 Silverman and co-workers [15] reported utilizing the ratio as an indication for operation. Baylen and associates [1] have described the usefulness of the left atrial and left ventricular end-diastolic diameters for detecting large left-to-right shunts.

The left atrial/aortic ratio was found to be very important in assessing the need for operation in these infants, especially when the presence of RDS made radiographic estimation of heart size difficult. It is possible to make an echocardiographic diagnosis of PDA 24 hours before physical findings make the diagnosis clear; the technique is useful in assessing the efficacy of treatment for congestive failure. There is good correlation between the left atrial/aortic ratio and the size of the ductus as measured during operation. In the patients in whom the ratio was less than 1.0, the ductus was found to be small and probably was not contributing to the patient's problems. After the PDA is ligated the ratio should return rapidly to normal, sometimes within an hour after operation.

Conclusions

Mortality rates for newborn infants with RDS (hyaline membrane disease) are 30 to 50% [2, 13]. Death is usually a result of oxygen toxicity and severe pulmonary disease. It is well known that premature infants who require mechanical ventilation and subsequently develop large shunting through a PDA have a poor prognosis (49% mortality in this study) and frequently die of complications related to prolonged respirator support.

Early surgical ligation of a large PDA in infants with respirator-dependent RDS is critical if these patients are to survive with normal lungs. Many clinicians take the attitude that infants with severe RDS are "too sick" to undergo surgical ligation, and choose medical therapy for varying lengths of time after the clinical OLS is observed. Indeed, the infant is too ill to *forego* operative closure of the ductus by this time. The operative risks reported using the extrapleural approach are minimal in nearly every series (none of the deaths in the studies examined were due to surgical complications), and others have reported equally excellent results with the transpleural method of ductal ligation. Hospital mortality with either technique for closure of uncomplicated PDA by experienced hands is essentially zero [7].

Echocardiography—specifically the left atrial/aortic root ratio—offers an accurate, inexpensive method for early determination of the OLS, before a murmur, bounding pulses, cardiomegaly, and increased pulmonary vascularity are present.

Infants with mild RDS or without RDS who develop a PDA can be managed medically until spontaneous closure occurs, elective operation is chosen, or operation becomes imperative due to persistent congestive heart failure and impending respiratory failure. If the severity of the RDS is in question or if the left atrial/aortic ratio is 1.0 to 1.2, medical treatment can safely be followed for 48 hours before deciding about the need for operation.

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Notice from the Southern Thoracic Surgical Association

The Twenty-third Annual Meeting of the Southern Thoracic Surgical Association will be held at the Princess Hotel, Acapulco, Mexico, on November 4–6, 1976. The scientific program will be published in the September issue of *The Annals of Thoracic Surgery*.

Applications for membership must be completed by September 1, 1976, and forwarded to Orin D. Butterick, M.D., 910 Madison Ave, Memphis, TN 38103.

Nonmember physicians are welcome to attend the meeting. There will be a $100 registration fee for nonmembers excluding interns, residents, authors in the program, invited speakers, and thoracic surgeons from Mexico. Do not write to the hotel for reservations. Applications for room and group plane reservations may be obtained from:

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134 Carondelet St
New Orleans, LA 70130

J. Kent Trinkle, M.D.
Secretary-Treasurer

Premature Infants with Patent Ductus Arteriosus and Respiratory Distress: Selection for Ductal Ligation

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J. Tracy Schreiber, M.D., Jens G. Rosenkrantz, M.D.,
Lester W. Martin, M.D., Barry G. Baylen, M.D.,
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ABSTRACT **Operative treatment of patent ductus arteriosus (PDA) in premature infants with respiratory distress has been advocated when rapid and favorable response to medical management has not occurred. At Cincinnati Children's Hospital from September, 1971, to January, 1975, 28 patients with respiratory distress syndrome (RDS) and PDA underwent ductal ligation after failing to respond to intensive medical management. There were 15 survivors and 13 deaths, for a survival rate of 53%.**

We have found the most reliable assessment of PDA and its response to medical management to be a reduction in left cardiac chamber size as evidenced by echocardiography. In 15 of the 28 infants who underwent ligation, echocardiography showed that they had failed to respond to medical management. Seven of the group survived.

During the same period 15 infants with RDS and PDA responded favorably to medical management and showed return of left cardiac chamber size to normal by serial echocardiograms. Of these, 11 survived and 4 died of noncardiac causes.

Clinical improvement was corroborated without exception by echocardiographic demonstration of a reduction in size of the left cardiac chamber. We believe that infants who follow this course should not have ductus ligation. We contend that the choice of surgical candidates should be more selective since a survival rate of only 50% has been obtained in this and other series. Further, we have found that only 8 of 14 long-term survivors in our series are free from pulmonary disease.

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Patent ductus arteriosus (PDA) was originally described by Gibson in 1900 [6]. It was successfully treated operatively by Gross and Hubbard in 1938 [7], and since then surgical closure of PDA has become a commonly practiced operation. The incidence of patent ductus in the general population is 0.04% in term infants at sea level [11] and 0.72% at high altitudes [13]. However, patent ductus occurs in 15% of premature infants [4, 10]. Many of these premature neonates also have respiratory distress syndrome (RDS) [15]. Surgical ligation of the patent ductus in such infants has been advocated in several recent reports [5, 8–10, 18], and the need for early diagnosis and operative intervention in those who do not show a favorable response to medical management has been stressed.

Our experience at the Cincinnati Children's Hospital with this important problem [2] prompted us to review our results. This experience along with a description of early diagnosis and follow-up evaluation of patent ductus by echocardiography form the basis of this report.

Materials and Methods

From September, 1971, through January, 1975, 28 infants with RDS and PDA underwent ductal ligation at the Cincinnati Children's Hospital. The clinical diagnosis of respiratory distress was made on the first day of life in all cases by the findings of apneic episodes, bradycardia, hypoxia, acidosis, and the presence of a diffuse reticulogranular pulmonary shadow on chest roentgenograms. Patent ductus was diagnosed clinically by a harsh systolic murmur that frequently extended into diastole and was most prominent over the midleft sternal border. There was also accentuation of peripheral pulses and widening of the pulse pressure. The diag-

Table 1. Data on the 28 Patients with Respiratory Distress Syndrome and Patent Ductus Arteriosus

Birth Weight (gm)	Male	Female	Approximate Gestational Age (wk)	Postnatal Age at Operation (days)
700–799	0	1	24	23
800–999	1	3	25–28	18–87
1,000–1,499	10	7	26–32	3–127
≥ 1,500	2	4	30–34	6–53

nosis was confirmed in each of the 28 infants at operation. As our experience evolved, the indications for operation varied but generally were persistence of signs of patent ductus, continued need for artificial ventilation, or worsening respiratory status as shown by serial blood gas determinations and radiographic evidence of progressive pulmonary deterioration. The composition of the group with details on weight, gestational age, and interval from birth to operation is given in Table 1.

Twenty infants were given digitalis when the clinical diagnosis of patent ductus or congestive heart failure was made, and 21 were given furosemide intermittently. Twenty-three patients were artificially ventilated preoperatively; this treatment started shortly after birth in most cases and was continued throughout the preoperative period, which varied from 3 to 113 days. Five infants did not require artificial ventilation at any time prior to ductus ligation. Four of the ventilated patients demonstrated radiographic evidence of cardiomegaly. Details relating to artificial ventilation and roentgenographically demonstrated cardiomegaly are listed in Table 2.

Echocardiography was employed during the last two years of the four-year period to evaluate patients with suspected patent ductus. Particular attention was paid to the estimated anteroposterior dimensions of the left atrium and left ventricle at the end of diastole. These chambers were considered enlarged when their measurements exceeded the mean plus 2 standard deviations for groups of infants studied at this institution with similar weights who did not have PDA [3]. Fifteen infants in this group of 28 underwent echocardiographic estimation of left atrial and ventricular size.

During the same period, 15 additional infants with RDS and the clinical diagnosis of PDA had echocardiograms and did not undergo ductal ligation, having improved clinically on medical management. This group of infants was used in our study to augment the data relative to left atrial and ventricular size and the influence of changes in these dimensions on indications for ductal ligation.

Table 2. Details on Artificial Ventilation and Cardiomegaly in 23 Patients

Day of Life Artificial Ventilation Was Initiated	Preoperative Ventilation Time (days)	Radiographic Evidence of Cardiomegaly
1	5	−
1	53	−
1	18	−
1	43	−
1	11	−
1	9	−
1	10	+
1	35	−
1	5	−
1	3	−
1	7	−
1	14	+
1	10	−
1	20	−
2	17	+
2	7	−
2	24	−
2	43	−
2	113	−
3	3	−
3	76	−
7	6	−
27	2	+

Results

Thirteen of the 28 babies (46%) undergoing ductal ligation died during initial hospitalization. Postmortem examination was obtained in 8 of them. Times of death are given in Table 3 along with mortality rates by birth weight. Causes of in-hospital death included: bronchopulmonary problems (6 infants); pneumonia or progressive RDS or both (7 infants); intracranial hemorrhage (3 infants); necrotizing enterocolitis (1 infant); and sepsis (1 infant). In several cases multiple causes were recognized. No deaths were directly attributed to operation. Surgical complications among the 13 babies dying in the hospital were confined to 1 patient who had acute hemorrhage from a small aortic branch with resultant transient shock.

Of the 15 infants discharged from the hospital alive, none had significant surgical complications. These babies were discharged 40 to 365 days postoperatively. Seven appeared to have significant residual pulmonary disease after discharge (roentgenographic changes consistent with bronchopulmonary dysplasia or chronic cor pulmonale necessitating digitalis therapy). One of these infants subsequently died 370 days postoperatively of acute respiratory insufficiency secondary to preexisting severe subglottic stenosis. Of the remaining 14 patients still alive at this time, 8 are free from pulmonary symptoms and 6 appear to have significant chronic lung disease.

Of the 15 infants who underwent echocardiography with subsequent ductal ligation, all showed persistent enlargement of the left cardiac chamber in the preoperative period, and all were judged at operation to have a PDA of significant size. Of the 15 infants undergoing echocardiography whose patent ductus was managed medically, all showed an initially enlarged left cardiac chamber that returned to normal with one to two weeks of medical therapy. Eleven of these infants improved and were discharged from the hospital with 2 still showing evidence of persistent patent ductus. Four of the 15 died 10 to 30 days after beginning medical therapy. In 2 of them postmortem examination demonstrated that the ductus was closed. The other 2 did not undergo postmortem examination, but it was certain that they died of noncardiac causes.

Table 3. Details on the 13 Hospital Deaths

Birth Weight (gm)	No. of Infants	In-Hospital Deaths	Time of Death (days postop)
700–799	1	0	
800–999	4	2	1, 51
1,000–1,499	17	9	1–370
⩾ 1,500	6	2	1, 3

Comment

Successful ligation of a PDA in the presence of RDS was described by Powell in 1963 [14]. Since that time, several reports have supported operative intervention as a means of relieving respiratory distress and preventing bronchopulmonary dysplasia [5, 8–10, 18].

Our patients have closely corresponded to those in other large groups reported. The premature infants we evaluated had RDS and gestational ages of 25 to 35 weeks with the majority at about 30 weeks. Their birth weights ranged from 700 to 2,300 gm with the majority being below 2,000 gm. The overall sex ratio has been approximately equal. This differs from the usual groups of patients with patent ductus without prematurity and RDS, in which a greater female-to-male ratio has been seen.

The diagnosis of RDS was made on the first day of life. The presence of appropriate clinical findings led to the identification of an associated patent ductus. Chest roentgenograms and electrocardiographic findings were of little value in early diagnosis.

Cardiac catheterization has established the diagnosis with a high degree of accuracy. However, occasional complications and the low incidence of associated cardiac anomalies has led to infrequent use of this method in most medical centers. Thibeault and co-workers [17] have recently demonstrated patent ductus in 46 premature infants with RDS by single-film aortography. The estimated left-to-right shunt through the ductus by aortogram correlated well with the heart size and the clinical diagnosis of heart failure. In 14 infants with heart failure the ductus was demonstrated before a murmur appeared.

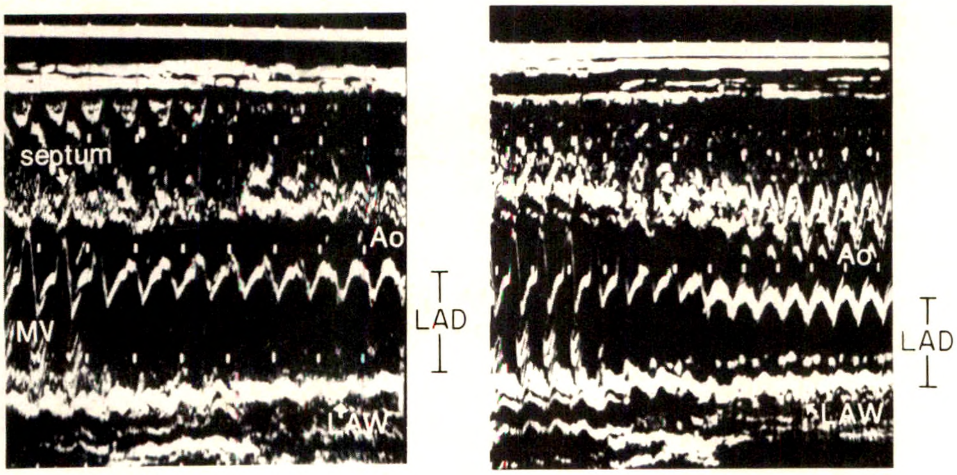
Echocardiography has proved to be a most dependable, safe, and rapid method of diagnosing a PDA in infants with RDS [12, 13, 16]. Left cardiac chamber enlargement is frequently found at the time a murmur is first heard. Serial evaluations are easily obtained, and a return of the left cardiac chamber size to normal with successful medical management or following ductal ligation has been consistently observed [13]. The Figure illustrates changes in dimensions in an infant who had abnormal preoperative measurements.

The indications for ductal ligation in babies with RDS have been failure of medical therapy to control congestive failure and deterioration of pulmonary function (increasing carbon dioxide retention, hypoxemia, and reduction in pulmonary compliance) [5, 8–12, 18]. In a recent report by Gay and associates [5], there were 30 survivors and 14 deaths in a group of respirator-dependent infants with PDA and RDS treated by ductal ligation, a 68% survival rate. In contrast, 15 infants not requiring artificial ventilation received ligation of the ductus with only 1 death, which was related to operation. Gay and his associates concluded that ductal ligation should be performed within 4 days of diagnosis to prevent bronchopulmonary dysplasia if a positive response to medical management is not obtained. In a similar series reported by Zachman and colleagues [18] a 60% incidence of bronchopulmonary dysplasia was found in the babies who died.

The survival rate in our group (53%) is similar to the rates given in other reports [5, 18]. However, the overall results in terms of mortality and quality of life among survivors have been unsatisfactory in our experience. Over the long term, 6 of our 14 long-term survivors have chronic lung disease, many with cor pulmonale. These results indicate that at present there is insufficient information on which to base proper patient selection for ligation. Apparently, many infants are operated on after irreversible effects have occurred in a compromised respiratory system. The exact mechanism by which a patent ductus affects pulmonary mechanics, gas exchange, and the development of bronchopulmonary dysplasia remains to be clarified. It is suspected that further pulmonary damage occurs after large left-to-right ductal shunts have caused left heart failure. Volume overload of the left atrium produces elevation of pulmonary venous and capillary pressures with resultant alveolar transudation and hypoventilation. A serious ventilation/perfusion disorder occurs, with reduction of lung compliance. This ultimately results in decreased oxygenation and further impairment of the stressed left ventricle.

Prevention of these complications will likely depend on earlier recognition and ligation of the patent ductus that is shunting a large volume

The left atrial dimension (LAD) *is reduced by one-third following ductal ligation in an infant.* (MV = *mitral valve;* LAW = *left atrial wall;* Ao = *aortic outflow tract.*)



Preoperative

24 hr Postoperative

from left to right [11]. It may be necessary to employ special methods for recognition. For example, aortography quite often can demonstrate a patent ductus before a murmur is evident. Certainly, earlier use of echocardiography shows much promise for demonstrating left chamber enlargement associated with patent ductus before clinical signs of cardiac decompensation occur [3, 16]. It should be possible to perform ductal ligation prior to the development of irreversible pulmonary changes. One would hope that an increase in immediate survival and preservation of cardiopulmonary function in the long term could then be accomplished in these seriously ill infants.

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The Ductus Debate: Ligation in Prematurity?

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ABSTRACT **This report describes 20 premature infants who have undergone surgical ligation of a patent ductus arteriosus (PDA), diagnosed solely by physical examination in all but 2 instances. There were no operative deaths. Eleven of these 20 infants had severe associated hyaline membrane disease (HMD) necessitating mechanical ventilatory support from the first or second day of life. Only 3 of these 11 infants (27%) ultimately survived to leave the hospital. In contrast, 8 of 9 premature neonates (89%) with severe congestive heart failure but without HMD were discharged alive.**

Surgical ligation of the PDA in a premature infant is an appropriate and successful mode of treatment when congestive heart failure is refractory to medical management. Proof is lacking, however, to establish the efficacy of PDA ligation in the premature infant with HMD.

Almost twenty-five years elapsed between the successful ligation of a patent ductus arteriosus (PDA) by Gross and Hubbard in 1938 [14] and the application of this operation to premature infants with hyaline membrane disease (HMD) by Powell in 1963 [25]. Numerous publications have recently summarized the results of ductus interruption in the premature infant [3, 4, 7, 9, 11, 12, 15–19, 22–24]; unfortunately, these reports have not clearly defined the indications for and usefulness of this procedure. Indications, diagnostic criteria, and timing of operation have varied widely. Randomization of patient selection has been ignored to date.

The incidence of persistent patency of the ductus arteriosus in premature infants is well established [1, 2, 6, 8, 10, 13, 21]. A further increased incidence is apparent in those infants surviving management of HMD and prematurity [19, 20, 27, 29].

Our experience indicates relatively distinct separation in both statistical survival and the quality of survival following PDA ligation between premature infants with congestive heart failure alone and those with HMD. This observation was also alluded to by Kitterman and associates [19] in a smaller series of infants in 1972 and has recently been substantiated by Coran and his co-workers [7]. This distinction should aid in the future selection of infants most likely to benefit from ductus ligation.

Materials and Methods

During the three-year period between May, 1972, and April, 1975, 1,640 infants were admitted to the Neonatal Intensive Care Unit at Jackson Memorial Hospital and the Department of Pediatrics of the University of Miami School of Medicine. Sixty-five percent weighed less than 2,500 gm at birth and 11% were less than 1,000 gm. Twenty-two percent were admitted primarily for the treatment of clinically and radiographically apparent HMD. The typical systolic murmur of a PDA was described in 3% at admission; murmurs subsequently became apparent in several more infants.

Congestive heart failure in these infants was characterized by tachypnea, tachycardia, edema, fluid retention, progressive hepatomegaly, progressive cardiomegaly, or radiographically apparent pulmonary edema. When it was associated with bounding peripheral pulses, a hyperactive precordium, a characteristic systolic murmur, and a widened umbilical arterial pulse pressure, the presence of a PDA with a large left-to-right shunt was suspected.

Medical management consisted of digitalization, fluid restriction, and intravenous adminis-

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tration of diuretics. Salt-poor albumin was given when total serum proteins were below 4 gm per 100 ml; anemia was corrected by administration of packed red blood cells. Umbilical arterial blood gases were monitored. Orotracheal intubation with continuous positive airway pressure or intermittent mandatory ventilation was used when ventilatory support was required.

Cardiac catheterization was carried out in only 1 of these infants suspected of having a PDA, the first child in the series. An isolated aortogram was obtained in another infant, utilizing the umbilical arterial catheter, and demonstrated the ductus as described in two recent reports [7, 11]. We have used the echocardiographic diameter of the left atrium compared with the diameter of the aorta, as described by Silverman [28] and Baylen [5] and their colleagues, as supportive evidence for a significant left-to-right shunt. The diagnosis of PDA was based on clinical and physical diagnostic grounds in all subsequent infants.

Twenty critically ill premature neonates failing to respond to medical management of congestive heart failure and requiring mechanical ventilatory support were referred for PDA ligation. These 20 infants have been retrospectively divided into two groups: Group A consists of 11 infants with HMD, PDA, and congestive heart failure; Group B consists of 9 with a PDA associated with refractory congestive heart failure but *without* preexisting HMD.

Respiratory distress and the need for ventilatory support were common to most infants. Weaning from the respirator had been attempted without success in those Group A infants in whom support had been required since birth. All infants in Group A were hypoxemic from birth, requiring mechanical ventilation from the first or second day of life (Fig 1).

A majority of infants in Group B, *without* HMD, eventually deteriorated to the point of requiring mechanical ventilatory assistance (Fig 2). Whereas Group A infants required institution of ventilatory support between the first and second day of life, those in Group B were ventilated for the first time at approximately 3 weeks of age. Infants in Group A required an average of twelve days of preoperative ventilatory support; Group B infants were ventilated for an average of three days preoperatively.

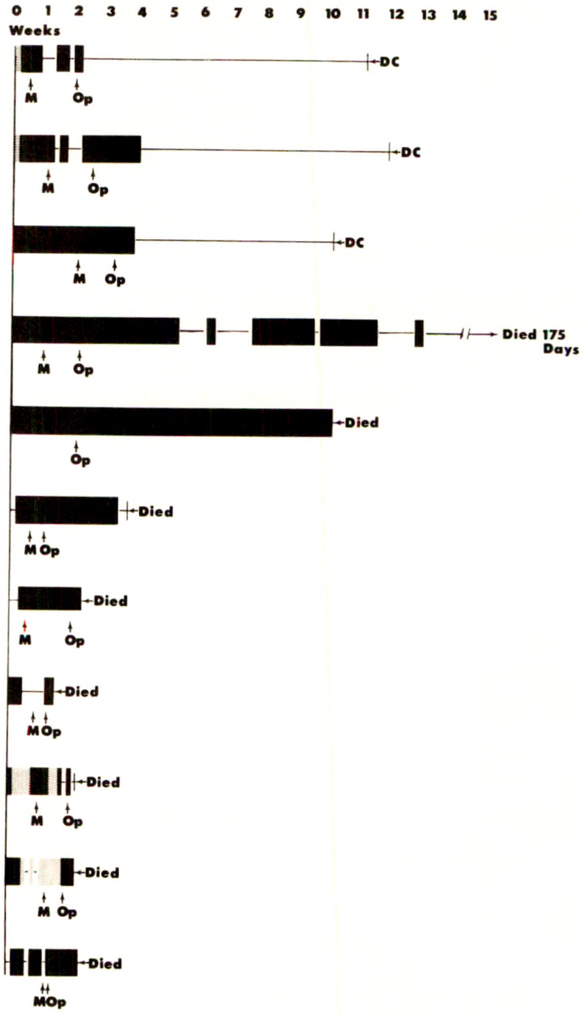

Fig 1. Time course of intubation and ventilatory support in Group A infants (HMD and congestive heart failure). Only the top 3 infants survived. Note that ventilatory support was required from virtually the first day of life in all these children. (Solid dark areas = *periods of intermittent positive-pressure ventilation;* dotted areas = *periods of continuous positive airway pressure through an orotracheal tube;* M = *time the murmur was first heard;* Op = *ductus ligation;* DC = *discharged alive;* Died = *hospital death.)*

The typical systolic murmur of a PDA in infants with elevated pulmonary arterial pressure was noted at about 1 week of age in Group A infants and somewhat later (12 days) in Group B. Other characteristics of these two groups are summarized in the Table.

Anesthesia consisted of oxygen, small quantities of nitrous oxide, muscle relaxants, and manual ventilation through an orotracheal tube.

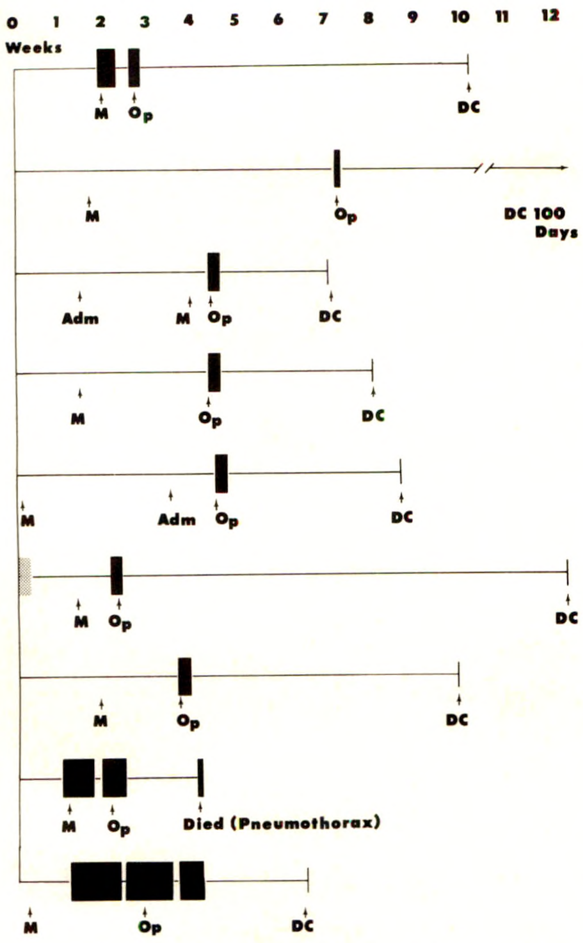

Fig 2. Time course of intubation and ventilatory support in Group B infants (PDA and congestive heart failure but no HMD). Note the much later initiation of respiratory support in these infants than in Group A neonates. Only 1 hospital death occurred in this group. (Key same as for Figure 1.)

The PDA was exposed through a posterolateral left transpleural thoracotomy in the third intercostal space and was doubly ligated. The thoracotomy, ductus ligation, and closure required between 10 and 20 minutes. Infants were transferred back to the Neonatal Intensive Care Unit for postoperative care.

Results

There were no intraoperative deaths in this series of 20 infants. Most hospital deaths occurred many days—even weeks—following operation. Two infants died within 24 hours following operation, 1 as a result of pneumothorax and the other with septicemia and central nervous system hemorrhage. Necrotizing enterocolitis, sepsis, and central nervous system hemorrhage were the predominant factors in the other 9 deaths.

Of the 11 infants in Group A with HMD and congestive heart failure, *only* 3 ultimately survived to be discharged from the hospital. Eight of the 9 infants in Group B with congestive heart failure refractory to medical management lived. The single death in this group was preventable—an unrecognized pneumothorax resulting in cardiac arrest.

Those infants who survived improved quickly, requiring an average of five days of postoperative ventilatory support compared with nineteen days for those who ultimately died. The average weight gain from operation until discharge for surviving infants was almost identical to that which one would expect for normal premature infants of equivalent gestational age (Fig 3).

All the surviving patients in these combined groups have progressed satisfactorily since discharge except for 1 infant, who has hydrocephalus requiring shunting. Psychometric assessment of the 11 surviving infants is in progress.

Comment

We have followed the conservative and noninvasive operative indications outlined by Murphy and his co-workers [23] with minor modifications. The presence of a PDA was suspected from auscultation several days before surgical intervention. Congestive heart failure unresponsive to digitalis and diuretics was apparent radiographically by cardiomegaly, increased pulmonary vascular markings, perihilar prominence, and in some cases frank pulmonary edema. Arterial blood gases indicated a progressively rising carbon dioxide tension. Two infants did not require ventilatory support until a short time before operation. Peripheral edema, periorbital edema, and hepatomegaly were present in some of these patients, although we have usually intervened surgically prior to the onset of these late manifestations of congestive heart failure.

Based on our experience with these 20 premature infants, we see no need for cardiac catheterization. The high incidence of complica-

Data on 20 Patients with Patent Ductus Arteriosus and Congestive Heart Failure

	Group A: HMD & CHF		Group B: CHF Only	
Factor	Survivors (N = 3)	Deaths (N = 8)	Survivors (N = 8)	Deaths (N = 1)
Sex	2M/1F	2M/6F	3M/5F	F
Gestation (wk)	32	31 (28–33)	30 (25–32)	28
Birth weight (kg)	1.6 (1.3–1.8)	1.3 (1.0–2.0)	1.2 (0.9–1.4)	0.8
First day of respiratory support	1	1.5 (1–3)	24 (1–51)	8
Preop respiratory support (days)	17 (10–23)	11 (4–16)	3 (1–11)	7
Day murmur first heard	9 (4–15)	6 (2–9)	12 (1–28)	9
Age at operation (days)	18 (14–23)	12 (8–16)	28 (16–51)	15
Weight at operation (kg)	1.4 (1.1–1.7)	1.2 (1.0–1.5)	1.2 (0.8–1.8)	0.7
Postop respiratory support (days)	5 (1–10)	19 (0–56)	2 (0–8)	3
Postop hospitalization (days)	59 (48–65)	33 (1–159)	40 (19–71)	14
Weight gain per day (gm)	21 (14–27)	7 (0–20)	23 (9–36)	9
Weight at discharge or death (kg)	2.7 (2.1–3.4)	1.4 (1.0–2.7)	2.1 (1.0–2.9)	0.8
Age at discharge or death (days)	77 (71–83)	46 (10–175)	68 (44–100)	29

HMD = hyaline membrane disease; CHF = congestive heart failure. Ranges in parentheses.

tions following catheterization described by Horsley and colleagues [16] and the low incidence of associated anomalies found by Edmunds [11] and Zachman [29] and their associates support our conservative approach.

Ligation of the PDA in each of these 20 infants resulted in obliteration of the murmur with no instance of recurrence. No other cardiac defects have been demonstrated among the survivors; no other cardiac anomalies were found in those infants who died and in whom postmortem examination was performed. When clinical findings are typical, cardiac catheterization is unnecessary and would add potential complication and delay.

The role of the patent ductus in the evolution of HMD remains undefined. Least tenable is the concept that ductus patency allows "decompression" of a hypertensive pulmonary vascular bed by means of a right-to-left shunt. Rudolph and colleagues [26] demonstrated *low* pulmonary and systemic arterial pressure in catheterizations performed on critically ill premature infants with HMD. Most of these infants had a predominant left-to-right shunt, although a mixed shunt was apparent in some. The indicator-dilution studies done by Coran and associates [7] support the data of Rudolph's group, the infants having had significant left-to-right shunts through the PDA.

The changing character of the ductus murmur reflects alterations in relative pulmonary and systemic vascular resistances, and perhaps changes in the ductus lumen itself. We lack hemodynamic proof of the magnitude of the left-to-right shunt in the infants described in this report, but all clinical findings point to a large aortic runoff into the pulmonary vascular bed.

It is unlikely that the role of the patent ductus in HMD can be resolved until noninvasive diagnostic methods establish the time course of in-

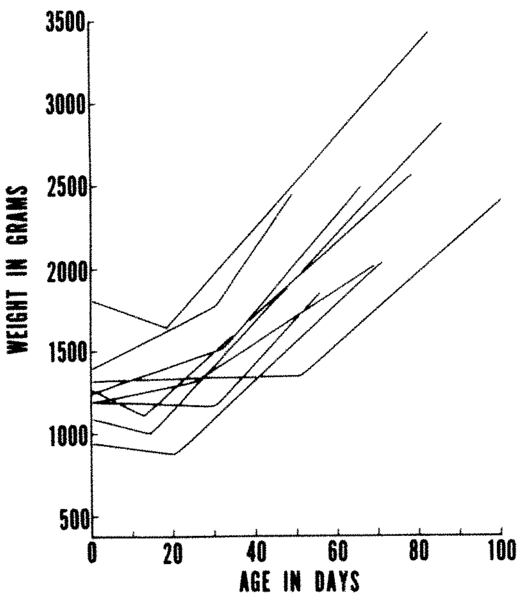

Fig 3. Weight gain before and after PDA ligation in premature infants with respiratory distress syndrome. Note the marked weight gain following PDA ligation in the surviving infants. (The points along the vertical axis indicate birth weights. The point at which the slope changes represents age and weight at operation. The right end of each line shows weight and age at discharge.)

creasing pulmonary blood flow and rising left atrial pressure. A multiinstitutional, randomized prospective study will be required before the therapeutic role of ductus ligation in premature infants with HMD can be established.

In contrast, ductus ligation *should* be carried out in the premature infant with congestive heart failure refractory to medical management who requires ventilatory assistance. The operative risk is low, and the heart failure can be controlled and the infant rapidly weaned from mechanical ventilatory support. Follow-up suggests nearly normal subsequent growth and development.

The low immediate operative mortality reported for premature infants with HMD and a PDA must not itself lead to the conclusion that ductus ligation is appropriate therapy. Proof of the efficacy of this procedure is lacking. While there are those who argue for earlier ductus ligation, even before the murmur and hyperdynamic circulatory signs of a large left-to-right shunt appear [7], we, like others, have seen infants with HMD and an unequivocal PDA in whom the PDA closed without operation.

Until definitive data are available, we advocate ductus ligation only in those premature infants who are ventilator dependent, demonstrate deteriorating pulmonary compliance, and, because of progressive congestive heart failure, retain fluid to a degree that forces their daily caloric intake below the minimum requirement necessary for anabolic weight gain. It is difficult to conceive of any beneficial role for the large PDA in these critically ill infants. The possibility remains that early PDA ligation may offer more benefit than waiting until the later, severe stage of the disease.

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Preferred Surgical Treatment for Alveolar Cell Carcinoma

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ABSTRACT **An analysis of our experience with 48 patients having bronchiolar or alveolar cell carcinoma is reported. The remarkable biological variability of this peripheral tumor has important surgical implications. Basically, two dominant clinical presentations occur. In the less common diffuse or multinodular form, prolonged survival is infrequent regardless of the therapeutic approach. Often these patients die from respiratory compromise due to the tumor itself. In the more common localized or solitary form the prognosis for cure is good, approximating 47% or higher. Based on the material presented, lobectomy is the preferred method of surgical treatment. In patients manifesting multinodular disease, surgical resection rarely seems warranted. The concept of preserving pulmonary tissue is stressed.**

Since its initial description by Malassez [11] in 1876, bronchiolar or alveolar cell carcinoma has been something of an enigma in the overall framework of bronchogenic carcinoma. Although metastatic glandular cancers manifest a similar histological appearance [14], most authors accept that this tumor's primary origin is the lung [1–3, 5, 8, 9]. Still, the specific site, cell, or mode of pathogenesis remains uncertain [10].

The remarkable biological variability exhibited by this peripheral tumor has important surgical implications. Basically, two dominant clinical presentations occur. In the less common diffuse or multinodular form (Fig 1), prolonged survival is unusual regardless of the therapeutic approach; these patients commonly die from respiratory compromise due to the tumor itself. Fortunately, the more frequent localized form arises as a solitary pulmonary nodule (Fig 2), for which the prognosis for cure is good. The distinction between the two clinical variants is not always clear, however, and patients with multinodular disease are sometimes subjected to harmful surgical resection. We have reviewed our experience with this disease in an attempt to determine a preferred method of management.

Clinical Material and Results

From 1954 through 1973, 58 patients with alveolar cell carcinoma were recorded in the tumor registries at Madigan, Fitzsimons, and Letterman Army Medical Centers. Although most of the tumors were confirmed initially by the Armed Forces Institute of Pathology, all records and available microscopical material were reexamined. Subsequently, 10 cases were excluded because of disagreement with the diagnoses or insufficient material for review. Therefore 48 cases, for an incidence of 3.1% among 1,553 patients with bronchogenic carcinoma, constitute the basis for this report. Interestingly, a previously reported patient with cavitary bronchiolar carcinoma associated with an intracavitary aspergilloma [12] was not included because of inability to substantiate this diagnosis. Men predominated by a ratio of 2.7 to 1 (35 to 13). Ages ranged from 28 to 77 years with a mean of 56.6 years. Of the 48 patients, 47 were white and 1 was black. Although a history of smoking was identified in 31 patients (64.6%), it was dis-

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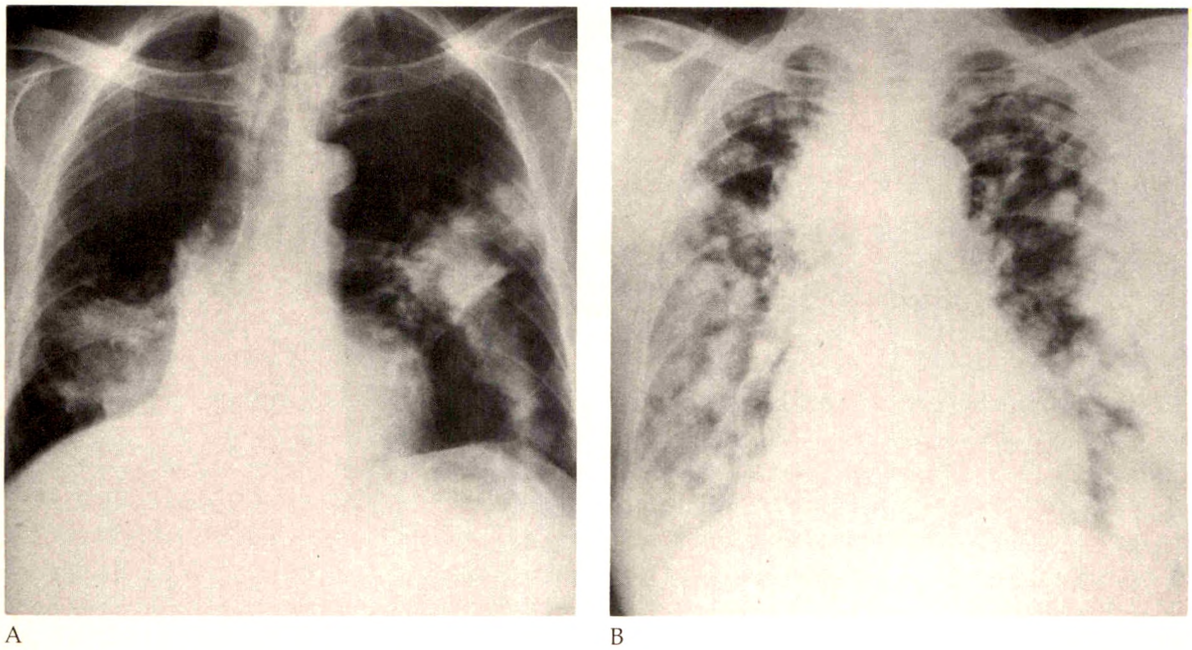
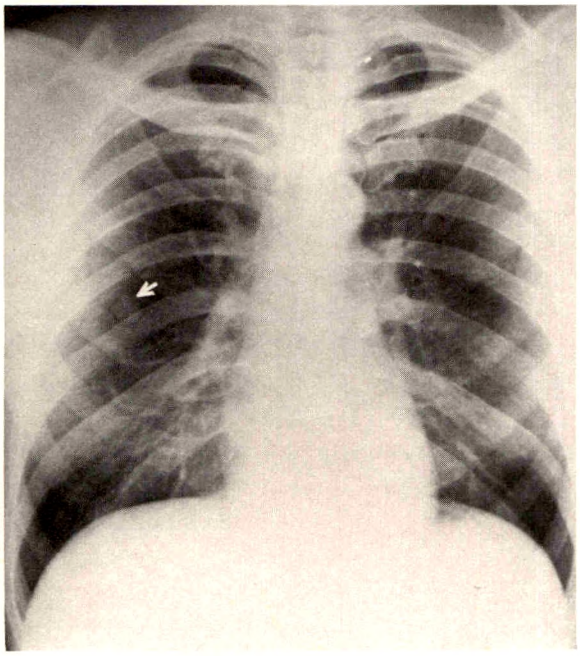


Fig 1. Abnormal chest roentgenograms showing (A) moderate bilateral multinodularity and (B) diffuse bilateral multinodularity.

Fig 2. Abnormal chest roentgenogram showing isolated peripheral nodule (arrow) *in right upper lobe. Patient is alive and free from disease 7 years, 9 months following lobectomy.*



tinctly absent in 5 (10.4%) and unknown in 12 others (25%).

Results of chest roentgenograms in 47 patients are categorized according to isolated or diffuse nodularity in Table 1. One patient died from an acute myocardial infarction before a chest roentgenogram was obtained, and alveolar cell carcinoma in the right upper lobe was an incidental finding at postmortem examination. In 35 cases (74.5%) a solitary peripheral lesion was either solid (20 patients, 57.1%), cavitary (1 patient, 2.9%), or infiltrative (14 patients, 40%) in appearance. Calcification was recognized in 2 of the 35 cases (5.7%). Nodule diameter was estimated in 13 patients only and varied from 1.4 to 7.0 cm with a mean size of 2.8 cm. Twenty-two nodules (62.9%) were situated in upper lobes, with the lower lobes next in frequency and the middle lobe and lingula least often involved. Finally, in 12 patients (25.5%) chest roentgenograms demonstrated evidence of either unilateral or bilateral diffuse nodularity that proved to be bilateral in the majority at postmortem examination.

Details of the clinical manifestations in these 48 patients are summarized in Table 2. Seventeen patients (35.4%) were asymptomatic. Frequently the alveolar cell carcinoma was identified during evaluation of another medical problem. A productive or dry cough occurred in

Table 1. Roentgenographic Findings in 47 Patients with Alveolar Cell Carcinoma

		Solitary Nodules (74.5%)			Diffuse Nodules (25.5%)	
Site of Nodules	No. of Patients	Solid	Cavitary	Infiltrative	Right Lung	Bilateral
RUL	13	8		5		
RML	3	3				
RLL	3	2		1		
LUL	9	3		6		
Lingula	2	2				
LLL	5	2	1	2		
	4				4	
	8					8
Total	47	20	1	14	4	8

RUL = right upper lobe; RML = right middle lobe; RLL = right lower lobe; LUL = left upper lobe; LLL = left lower lobe.

22 instances (45.8%); chest pain in 12 (25%); dyspnea in 10 (20.8%); and hemoptysis in only 4 (8.3%). Upper respiratory tract infection or pneumonia was a significant clinical feature in 10 instances (20.8%). Symptoms or signs related to the tumor portended an ominous outlook. However, 1 patient with initially localized disease survived longer than five years without treatment and during the last two years was known to have metastatic disease (Fig 3).

Multiple diagnostic methods were of variable success. Sputum cytology produced a positive yield in 7 of 43 patients (16.3%) and bronchoscopy was diagnostic in 4 of 34 (11.8%). With the suggestion of adenopathy, supraclavicular or scalene node biopsy yielded positive results in 3 of 8 cases (37.5%). In 3 patients with pleural effusions, cytology or pleural biopsy was highly suspicious for malignancy in 2 instances (66.7%). Mediastinoscopy provided a positive biopsy the single time it was employed. Nine patients had their alveolar cell carcinoma first documented at postmortem examination.

Table 2. Clinical Manifestations in 48 Patients with Alveolar Cell Carcinoma

Sign or Symptom	No. of Patients[a]
Asymptomatic	17
Chest pain	12
Productive cough	14
Dry cough	8
Dyspnea	10
Weight loss	8
Pneumonia	5
Hemoptysis	4
Upper respiratory infection	5
Pleural effusion	4
Anorexia	2
Cachexia	1
Hoarseness	1
Bone pain	1
Fatigue	1

[a] Several patients exhibited multiple signs or symptoms.

Primarily on the basis of infiltrative characteristics on chest roentgenograms, a presumptive diagnosis of tuberculosis was made in 7 patients (14.6%). Antituberculosis treatment was utilized in all 7, and 3 subsequently had positive cultures for mycobacteria coexistent with alveolar cell carcinoma. Another 4 patients (8.3%) had carcinomas identified in association with nonspecific pulmonary scars. Additionally, 2 patients (4.2%) exhibited hamartomas in close proximity to carcinomas in the upper lobes, and another patient (2.1%) had a closely associated sarcoid granuloma. Altogether, 10 of the 48 patients (20.8%) demonstrated alveolar cell carcinoma in areas of coexistent or previously diseased lung.

Thirty-seven operations were performed in 35 patients (Table 3) with 1 operative death (2.9%). This resulted from respiratory insufficiency on the thirty-seventh postoperative day following right pneumonectomy in a patient with the mul-

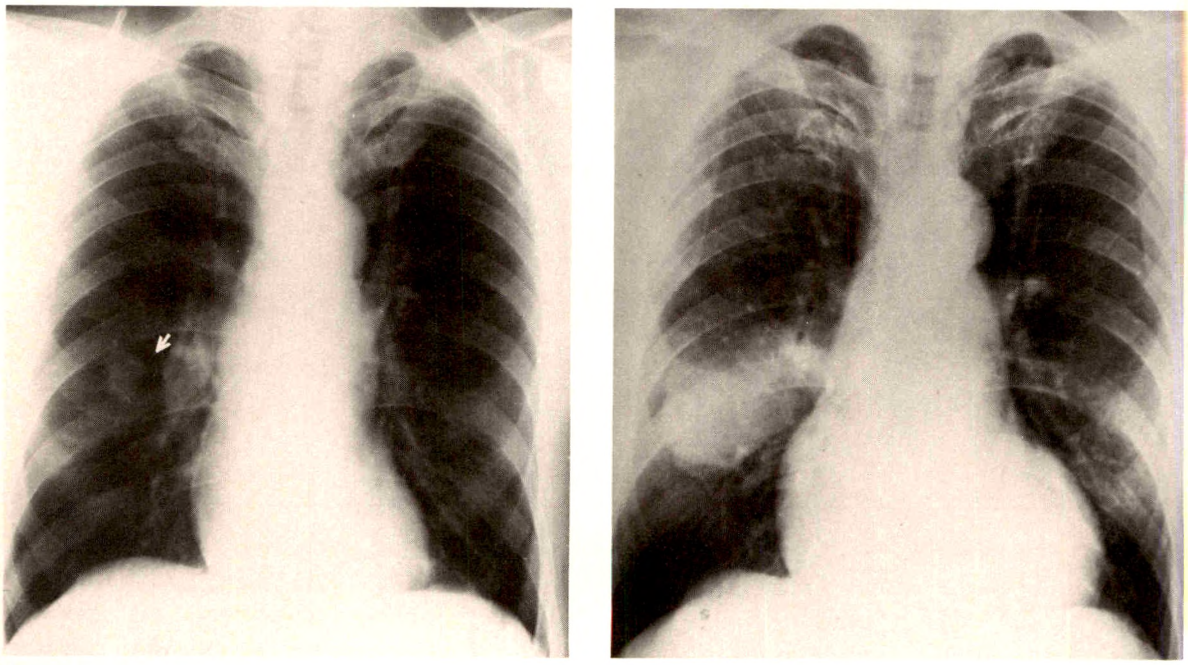


Fig 3. (A) Abnormal chest roentgenogram showing isolated peripheral nodule (arrow) *in right midlung field. (B) Chest roentgenogram two and one-half years later shows multinodularity. This patient survived five years without any form of treatment.*

Table 3. Results of 37 Operations in 35 Patients

Operative Procedure	No. of Operations
RU lobectomy	12
LU lobectomy	5
LL lobectomy	2
RM & RL bilobectomy	4
RL lobectomy	2
RM lobectomy	2
RU & RM bilobectomy	1
R pneumonectomy	1
Wedge resection, LLL	2
Wedge resection, RUL	1
Thoracotomy, biopsy only	5

RU = right upper; LU = left upper; LL = left lower; RM = right middle; RL = right lower; R = right.

tinodular form of the disease. Unsuccessful second surgical procedures for residual carcinoma consisted of wedge resection of the opposite upper lobe after an initial left upper lobectomy and completion pneumonectomy following an initial right lower lobectomy. Both patients experienced progressive respiratory impairment, and their survival was extended for only a matter of months.

Of the entire 48 patients, 13 (27.1%) survived five years or longer and were ostensibly cured (Table 4, Groups B and F). After resection of isolated peripheral nodules, 2 of them died from coronary occlusion without detectable cancer at 84 and 85 months, respectively. In addition, 2 others succumbed to subsequent primary bronchogenic carcinomas of different histology (undifferentiated and mixed adenosquamous) at 89 and 132 months, respectively (Group F). Therefore 9 patients (18.8%) remained alive and cured 60 to 144 months following lobectomy (Group B). Also, 4 patients (8.3%) were alive at 3 to 29 months without evident disease (Group C). One patient initially diagnosed at thoracotomy and biopsy only as manifesting pulmonary adenomatosis [15] remained alive at 50 months with diffuse disease. This patient reflects reasonable survival with diffuse disease when critical pulmonary tissue is not resected. The 12

Table 4. Outcome in 48 Patients with Alveolar Cell Carcinoma

Result	No. of Patients
A: Alive with disease	1
B: Alive without disease (over 5 years)	9
C: Alive without disease (under 5 years)	4
D: Dead with disease (related)	24
E: Dead with disease (unrelated)	4
F: Dead without disease (over 5 years)	4
G: Dead without disease (under 5 years)	2

patients who had multinodular disease roentgenographically when they were first seen died within relatively short intervals following diagnosis except for the one who progressed from localized to diffuse disease after three years. In several cases the diagnosis of diffuse alveolar cell carcinoma was suspected but not proved until after death.

Of the 35 patients with roentgenographically apparent isolated peripheral nodules, the diagnosis was an incidental postmortem finding in 2 who died from other disease processes (Group E). Excluding these 2 patients and the individual misdiagnosed as having pulmonary adenomatosis, the 13 long-term survivors signify a five-year survival rate of 40.6% (13 of 32) among patients with disease that was favorable roentgenographically. If 2 additional patients (Group G) are included who had no residual cancer when examined postmortem and who died of suicide and a myocardial infarction at 5 and 25 months, respectively, the total number cured in this category totals 15 of 32 patients (46.9%).

Comment

Reports from the Armed Forces Institute of Pathology frequently emphasize that alveolar cell carcinoma is most often first seen as a solitary pulmonary lesion. With localized disease, curative resection should afford excellent survival [2, 6]. In contrast, patients with multinodular disease seldom benefit from surgical intervention [2, 4, 8, 13]. Their ultimate fate often makes the preservation of pulmonary tissue an important concept. An analysis of the cancer-related deaths (Table 4, Group D) reveals that 11 of these 24 patients (45.8%) progressed to terminal respiratory impairment. Three others (12.5%) manifested pericardial metastases and cardiac tamponade as the primary cause of death. In patients demonstrating more than localized disease at thoracotomy, survival was adversely influenced by any form of extended resection (ie, bilobectomy, pneumonectomy, completion pneumonectomy). All these patients died from their disease, and residual pulmonary cancer was proved postmortem.

Two biological features favoring cure in alveolar cell carcinoma are the potential for slow growth and the tendency for the tumor to remain localized [1, 15, 16]. Once lymph node permeation takes place or satellite lesions appear, the likelihood of a favorable outcome is remote. Although isolated metastases to the same lung occur, this usually implies spread to the opposite lung and more distant sites. For proper surgical treatment, it is important to distinguish localized and curable disease from its multinodular and probably incurable counterpart. In patients with multinodular disease that remains unrecognized until thoracotomy, surgical resection becomes a matter of combined philosophy and experience. Certainly the results recorded in this series and by Fitzpatrick and colleagues [6] suggest that resections in excess of lobectomy are rarely indicated; actually, by removing critical pulmonary tissue, they may prove harmful. All patients who were cured in either series underwent lobectomy for localized peripheral disease.

We recommend an aggressive attitude toward undiagnosed solitary pulmonary lesions whether they are solid, cavitary, or infiltrative in appearance. Alveolar cell carcinoma in association with previous, suspected, or coexistent pulmonary disease occurred in 10 (20.8%) of our patients. Inflammatory or scarring conditions of the lung exhibiting roentgenographic progression should arouse the suspicion of malignancy. Noninvasive mediastinal laminagrams [7] are useful in assessing the status of the mediastinum. Frequently we add full-lung laminagrams of the lesion to check for additional disease. Eventually many patients with solitary peripheral carcinomas require thoracotomy for diagnosis. For disease that is benign grossly a wedge resection is performed for histological examination, followed by lobectomy if the lesion proves to be malignant. However, most patients undergo immediate lobectomy as the initial and only operative procedure. In patients demonstrating more than one pulmonary nodule, pleural seeding, or mediastinal tumor extension, biopsy alone is performed. In most instances these features indicate a behavioral alteration inconsistent with surgical cure. In addition, the quality of survival is improved with the preservation of pulmonary tissue.

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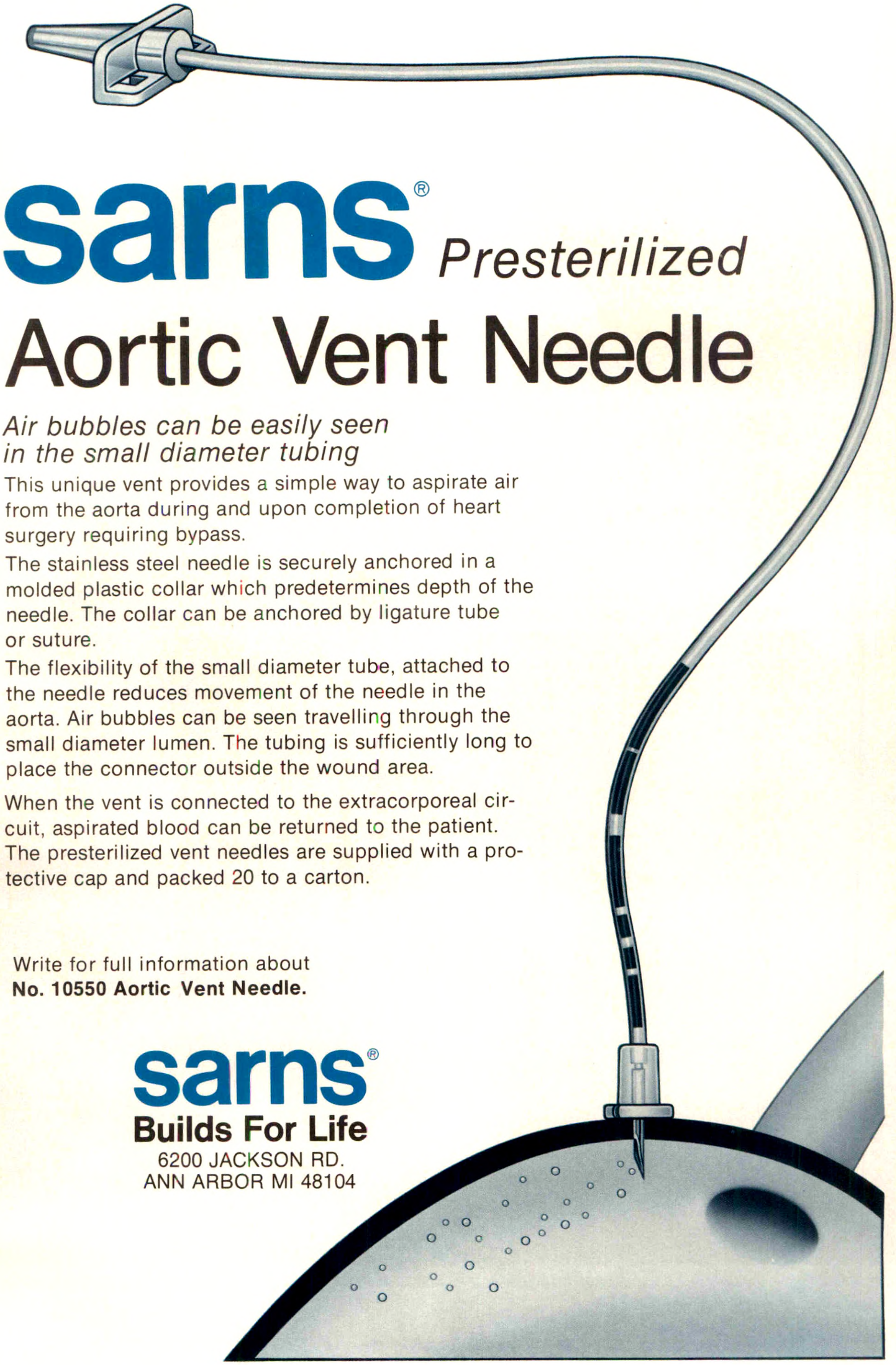

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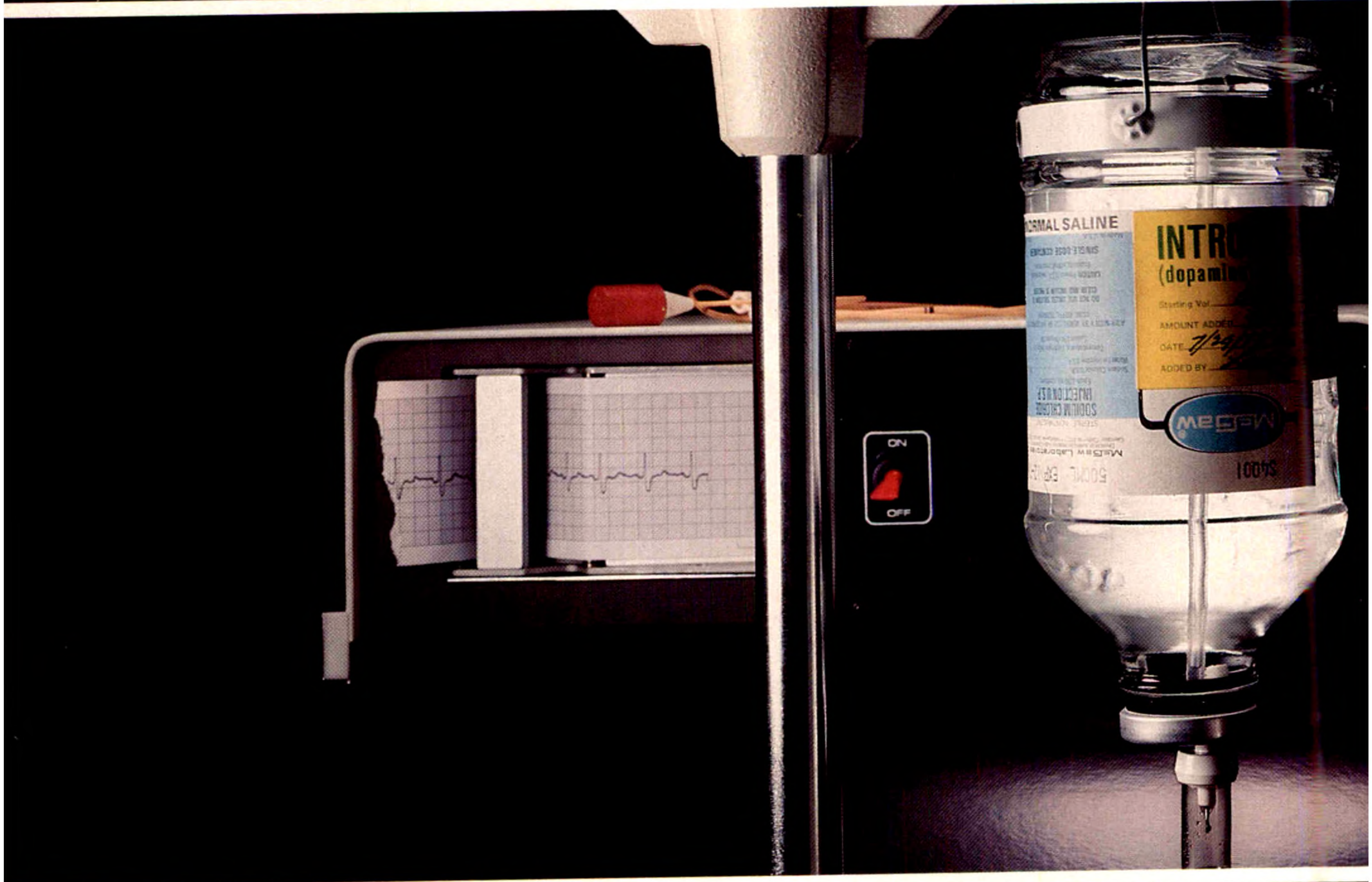

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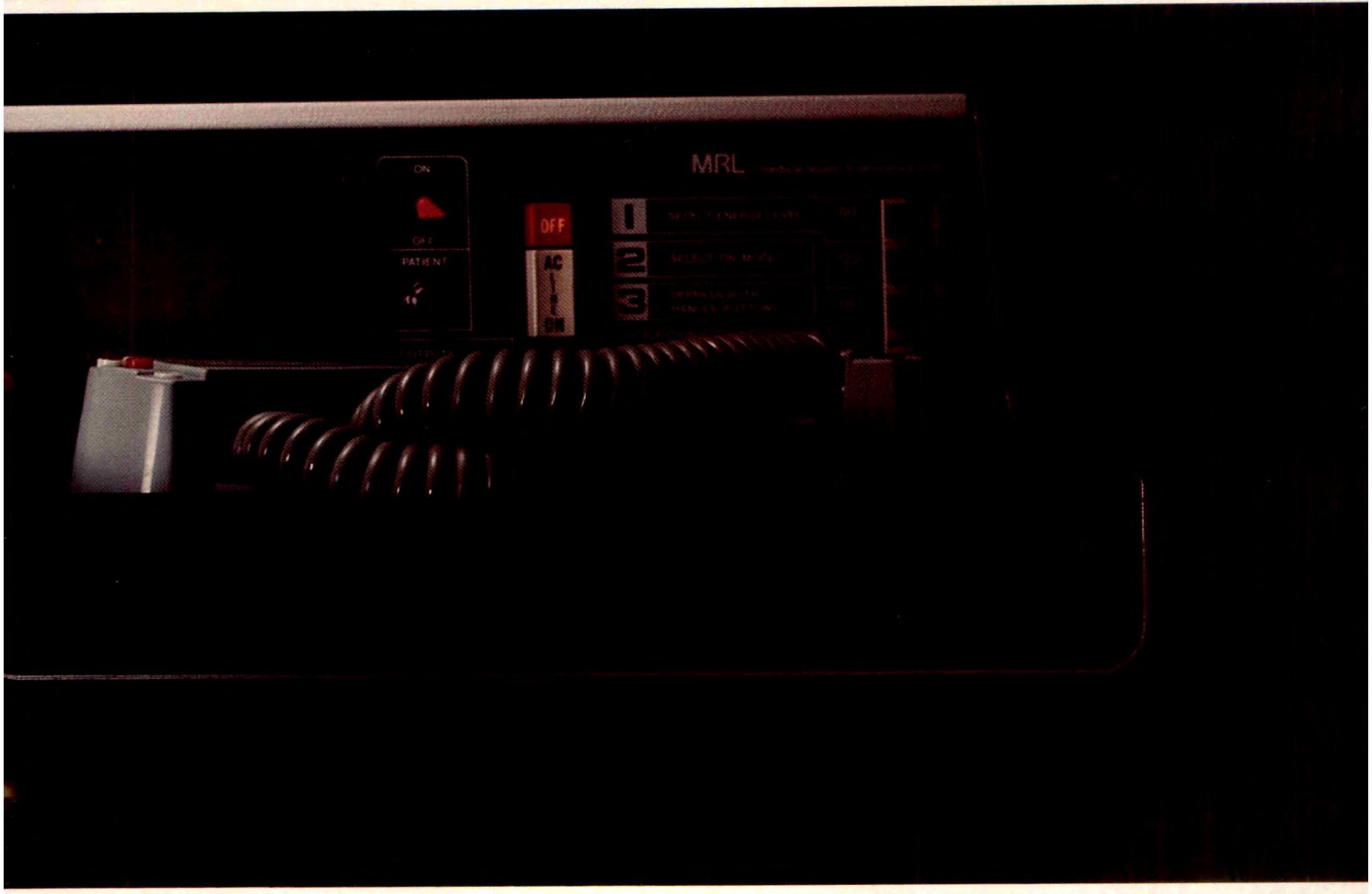

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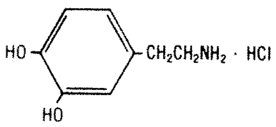

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ACTIONS: INTROPIN exerts an inotropic effect on the myocardium resulting in an increased cardiac output. INTROPIN produces less increase in myocardial oxygen consumption than isoproterenol and its use is usually not associated with a tachyarrhythmia. Clinical studies indicate that INTROPIN usually increases systolic and pulse pressure with either no effect or a slight increase in diastolic pressure. Total peripheral resistance at low and intermediate therapeutic doses is usually unchanged. Blood flow to peripheral vascular beds may decrease while mesenteric flow increases. INTROPIN has also been reported to dilate the renal vasculature presumptively by activation of a ''dopaminergic'' receptor. This action is accompanied by increases in glomerular filtration rate, renal blood flow, and sodium excretion. An increase in urinary output produced by dopamine is usually not associated with a decrease in osmolality of the urine.

INDICATIONS: INTROPIN is indicated for the correction of hemodynamic imbalances present in the shock syndrome due to myocardial infarctions, trauma, endotoxic septicemia, open heart surgery, renal failure, and chronic cardiac decompensation as in congestive failure.

Where appropriate, restoration of blood volume with a suitable plasma expander or whole blood should be instituted or completed prior to administration of INTROPIN.

Patients most likely to respond adequately to INTROPIN are those in whom physiological parameters, such as urine flow, myocardial function, and blood pressure, have not undergone profound deterioration. Multiclinic trials indicate that the shorter the time interval between onset of signs and symptoms and initiation of therapy with volume correction and INTROPIN, the better the prognosis.

Poor Perfusion of Vital Organs—Urine flow appears to be one of the better diagnostic signs by which adequacy of vital organ perfusion can be monitored. Nevertheless, the physician should also observe the patient for signs of reversal of confusion or comatose condition. Loss of pallor, increase in toe temperature, and/or adequacy of nail bed capillary filling may also be used as indices of adequate dosage. Clinical studies have shown that when INTROPIN is administered before urine flow has diminished to levels approximately 0.3 ml./minute, prognosis is more favorable. Nevertheless, in a number of oliguric or anuric patients, administration of INTROPIN has resulted in an increase in urine flow which in some cases reached normal levels. INTROPIN may also increase urine flow in patients whose output is within normal limits and thus may be of value in reducing the degree of pre-existing fluid accumulation. It should be noted that at doses above those optimal for the individual patient, urine flow may decrease, necessitating reduction of dosage. Concurrent administration of INTROPIN and diuretic agents may produce an additive or potentiating effect.

Low Cardiac Output—Increased cardiac output is related to INTROPIN's direct inotropic effect on the myocardium. Increased cardiac output at low or moderate doses appears to be related to a favorable prognosis. Increase in cardiac output has been associated with either static or decreased systemic vascular resistance (SVR). Static or decreased SVR associated with low or moderate increments in cardiac output is believed to be a reflection of differential effects on specific vascular beds with increased resistance in peripheral beds (e.g. femoral) and concomitant decreases in mesenteric and renal vascular beds. Redistribution of blood flow parallels these changes so that an increase in cardiac output is accompanied by an increase in mesenteric and renal blood flow. In many instances the renal fraction of the total cardiac output has been found to increase. Increase in cardiac output produced by INTROPIN is not associated with substantial decreases in systemic vascular resistance as may occur with isoproterenol.

Hypotension—Hypotension due to inadequate cardiac output can be managed by administration of low to moderate doses of INTROPIN, which have little effect on SVR. At high therapeutic doses, INTROPIN's alpha adrenergic activity becomes more prominent and thus may correct hypotension due to diminished SVR. As in the case of other circulatory decompensation states, prognosis is better in patients whose blood pressure and urine flow have not undergone profound deterioration. Therefore, it is suggested that the physician administer INTROPIN as soon as a definite trend toward decreased systolic and diastolic pressure becomes evident.

CONTRAINDICATIONS: INTROPIN should not be used in patients with pheochromocytoma.

WARNINGS: INTROPIN should not be administered in the presence of uncorrected tachyarrhythmias or ventricular fibrillation.

Do **NOT** add INTROPIN to any alkaline diluent solution, since the drug is inactivated in alkaline solution.

Patients who have been treated with monamine oxidase (MAO) inhibitors prior to the administration of INTROPIN will require substantially reduced dosage. Dopamine is metabolized by MAO, and inhibition of this enzyme prolongs and potentiates the effect of INTROPIN. The starting dose in such patients should be reduced to at least one-tenth (1/10) of the usual dose.

Usage in Pregnancy—Animal studies have revealed no evidence of teratogenic effects from INTROPIN. In one study, administration of INTROPIN to pregnant rats resulted in a decreased survival rate of the newborn and a potential for cataract formation in the survivors. The drug may be used in pregnant women when, in the judgment of the physician, the expected benefits outweigh the potential risk to the fetus.

Usage in Children—The safety and efficacy of this drug in children has not been established. INTROPIN has been used in a limited number of pediatric patients, but such use has been inadequate to fully define proper dosage and limitations for use. Further studies are in progress.

PRECAUTIONS: Avoid Hypovolemia—Prior to treatment with INTROPIN, hypovolemia should be fully corrected, if possible, with either whole blood or plasma as indicated.

Decreased Pulse Pressure—If a disproportionate rise in the diastolic pressure (i.e. a marked decrease in the pulse pressure) is observed in patients receiving INTROPIN, the infusion rate should be decreased and the patient observed carefully for further evidence of predominant vasoconstrictor activity, unless such an effect is desired.

Extravasation—INTROPIN should be infused into a large vein whenever possible to prevent the possibility of extravasation into tissue adjacent to the infusion site. Extravasation may cause necrosis and sloughing of surrounding tissue. Large veins of the antecubital fossa are preferred to veins in the dorsum of the hand or ankle. Less suitable infusion sites should be used only if the patient's condition requires immediate attention. The physician should switch to more suitable sites as rapidly as possible. The infusion site should be continuously monitored for free flow.

Occlusive Vascular Disease—Patients with a history of occlusive vascular disease (for example, atherosclerosis, arterial embolism, Raynaud's disease, cold injury, diabetic endarteritis, and Buerger's disease) should be closely monitored for any changes in color or temperature of the skin in the extremities. If a change in skin color or temperature occurs and is thought to be the result of compromised circulation to the extremities, the benefits of continued INTROPIN infusion should be weighed against the risk of possible necrosis. This condition may be reversed by either decreasing or discontinuing the rate of infusion.

> **IMPORTANT—Antidote for Peripheral Ischemia: To prevent sloughing and necrosis in ischemic areas, the area should be infiltrated as soon as possible with 10 to 15 ml. of Saline solution containing from 5 to 10 mg. of Regitine® (brand of phentolamine), an adrenergic blocking agent. A syringe with a fine hypodermic needle should be used, and the solution liberally infiltrated throughout the ischemic area. Sympathetic blockade with phentolamine causes immediate and conspicuous local hyperemic changes if the area is infiltrated within 12 hours. Therefore, phentolamine should be given as soon as possible after the extravasation is noted.**

Avoid Cyclopropane or Halogenated Hydrocarbon Anesthetics—Cyclopropane or halogenated hydrocarbon anesthetics increase cardiac autonomic irritability and therefore may sensitize the myocardium to the action of certain intravenously administered catecholamines. This interaction appears to be related both to pressor activity and to beta adrenergic stimulating properties of these catecholamines. Therefore, as with certain other catecholamines, and because of the theoretical arrhythmogenic potential, INTROPIN should be used with EXTREME CAUTION in patients inhaling cyclopropane or halogenated hydrocarbon anesthetics.

Careful Monitoring Required—Close monitoring of the following indices—urine flow, cardiac output and blood pressure—during INTROPIN infusion is necessary as in the case of any adrenergic agent.

ADVERSE REACTIONS: The most frequent adverse reactions observed in clinical evaluation of INTROPIN included ectopic beats, nausea, vomiting, tachycardia, anginal pain, palpitation, dyspnea, headache, hypotension, and vasoconstriction. Other adverse reactions which have been reported infrequently were aberrant conduction, bradycardia, piloerection, widened QRS complex, azotemia, and elevated blood pressure.

DOSAGE AND ADMINISTRATION:

WARNING: This is a potent drug: It must be diluted before administration to patient.

Suggested Dilution—Transfer contents of one ampul (5 ml. containing 200 mg. INTROPIN) by aseptic technique to either a 250 ml. or 500 ml. bottle of one of the following sterile intravenous solutions:

1) Sodium Chloride Injection, USP
2) Dextrose 5% Injection, USP
3) Dextrose (5%) and Sodium Chloride (0.9%) Injection, USP
4) 5% Dextrose in 0.45% Sodium Chloride Solution
5) Dextrose (5%) in Lactated Ringer's Solution
6) Sodium Lactate (1/6 Molar) Injection, USP
7) Lactated Ringer's Injection, USP

These dilutions will yield a final concentration for administration as follows:
250 ml. dilution contains 800 mcg./ml. of INTROPIN
500 ml. dilution contains 400 mcg./ml. of INTROPIN

INTROPIN has been found to be stable for a minimum of 24 hours after dilution in the sterile intravenous solutions listed above. However, as with all intravenous admixtures, dilution should be made just prior to administration.

Do **NOT** add INTROPIN Injection to 5% Sodium Bicarbonate or other alkaline intravenous solutions, since the drug is inactivated in alkaline solution.

Rate of Administration—INTROPIN, after dilution, is administered intravenously through a suitable intravenous catheter or needle. An i.v. drip chamber or other suitable metering device is essential for controlling the rate of flow in drops/minute. Each patient must be individually titrated to the desired hemodynamic and/or renal response with INTROPIN. In titrating to the desired increase in systolic blood pressure, the optimum dosage rate for renal response may be exceeded, thus necessitating a reduction in rate after the hemodynamic condition is stabilized.

Administration at rates greater than 50 mcg./kg./min. have safely been used in advanced circulatory decompensation states. If unnecessary fluid expansion is of concern, adjustment of drug concentration may be preferred over increasing the flow rate of a less concentrated dilution.

Suggested Regimen:

1. When appropriate, increase blood volume with whole blood or plasma until central venous pressure is 10 to 15 cm H_2O or pulmonary wedge pressure is 14-18 mm Hg.
2. Begin administration of diluted solution at doses of 2-5 mcg./kg./minute INTROPIN in patients who are likely to respond to modest increments of heart force and renal perfusion.

   In more seriously ill patients, begin administration of diluted solution at doses of 5 mcg./kg./minute INTROPIN and increase gradually using 5 to 10 mcg./kg./minute increments up to 20 to 50 mcg./kg./minute as needed. If doses of INTROPIN in excess of 50 mcg./kg./minute are required, it is suggested that urine output be checked frequently. Should urine flow begin to decrease in the absence of hypotension, reduction of INTROPIN dosage should be considered. Multiclinic trials have shown that more than 50% of the patients were satisfactorily maintained on doses of INTROPIN less than 20 mcg./kg./minute. In patients who do not respond to these doses with adequate arterial pressures or urine flow, additional increments of INTROPIN may be employed in an effort to produce an appropriate arterial pressure and central perfusion.
3. Treatment of all patients requires constant evaluation of therapy in terms of the blood volume, augmentation of myocardial contractility, and distribution of peripheral perfusion. Dosage of INTROPIN should be adjusted according to the patient's response, with particular attention to diminution of established urine flow rate, increasing tachycardia or development of new dysrhythmias as indices for decreasing or temporarily suspending the dosage.
4. As with all potent intravenously administered drugs, care should be taken to control the rate of administration so as to avoid inadvertent administration of a bolus of drug.

OVERDOSAGE: In case of accidental overdosage, as evidenced by excessive blood pressure elevation, reduce rate of administration or temporarily discontinue INTROPIN until patient's condition stabilizes. Since INTROPIN's duration of action is quite short, no additional remedial measures are usually necessary. If these measures fail to stabilize the patient's condition, use of the short-acting alpha adrenergic blocking agent, phentolamine, should be considered.

HOW SUPPLIED: 5 ml. ampuls containing 40 mg. dopamine HCl per milliliter.

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The open chest. Another opening for staph*?

ostoperative surgical infections
alve replacement: a procedure that can at nce sustain life *and* predispose to infection. lthough identification of the infectious rganism may be difficult, a delay in treatment ould result in invasion of the endocardium. he implicated organism may be a penicillinase-roducing staph. Progression can be swift nd devastating.

nitial antistaph therapy: injection
t's vitally important that effective treatment of acterial invasion begin as soon as possible. f you suspect the presence of staph and must egin therapy before definitive culture results re known, Injection Unipen® (nafcillin sodium)† is a particularly suitable agent.

Appropriate specimens for bacteriologic studies to determine the causative organisms and their susceptibility to nafcillin should be taken prior to the first dose of antibiotic.† And, if those studies subsequently implicate organisms other than penicillinase-producing staphylococci sensitive to nafcillin, discontinue it and administer the appropriate antibiotic.

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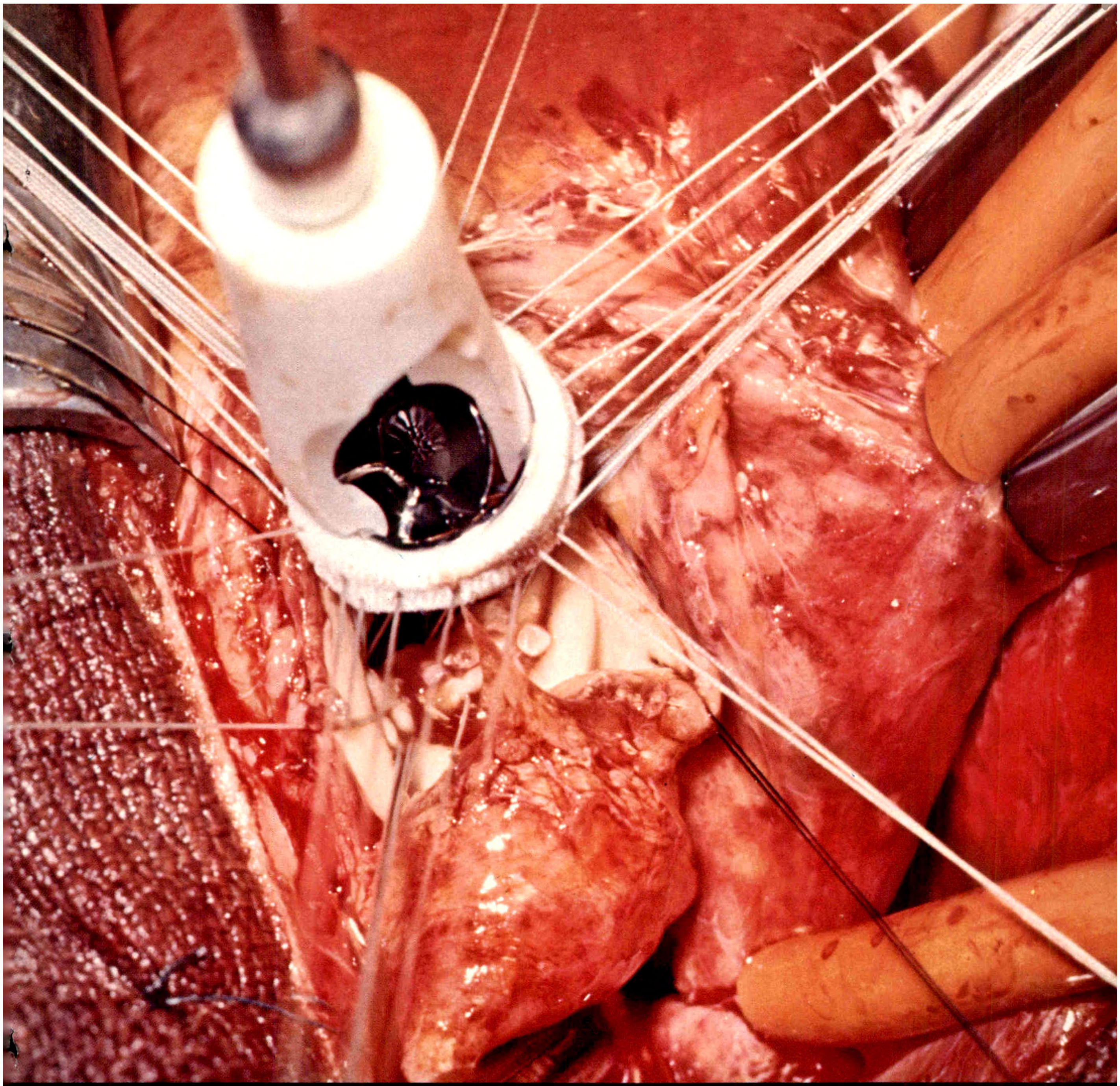
Unipen appears rapidly in plasma following intramuscular administration. Penetrates body tissues in high concentrations and diffuses well into pleural, pericardial and synovial fluids.



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continue antistaph therapy with the same anti-
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fcillin-susceptible penicillinase-producing staphylococci.
e Important Note on next page.
e important information under Parenteral Administra-
n on next page.

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See important information on next page

Unipen®
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AS THE MONOHYDRATE, BUFFERED, WYETH

Disc Susceptibility Tests: Quantitative methods that require measurement of zone diameters give the most precise estimates of antibiotic susceptibility. One such procedure* has been recommended for use with discs for testing susceptibility to penicillinase-resistant penicillin-class antibiotics. Interpretations correlate diameters on the disc test with MIC values for penicillinase-resistant penicillins. With this procedure, a report from the laboratory of "susceptible" indicates that the infecting organism is likely to respond to therapy. A report of "resistant" indicates that the infecting organism is not likely to respond to therapy. A report of "intermediate susceptibility" suggests that the organism would be susceptible if high dosage is used, or if the infection is confined to tissues and fluids (e.g., urine) in which high antibiotic levels are attained.

*Bauer, A.W., Kirby, W.M.M., Sherris, J.C., and Turck, M.: Antibiotic Testing by a Standardized Single-Discs Method, Am. J. Clin. Pathol., 45:493, 1966; Standardized Disc Susceptibility Test, FEDERAL REGISTER 37:20527-29, 1972.

Indications: Although the principal indication for nafcillin sodium is in the treatment of infections due to penicillinase-producing staphylococci, it may be used to initiate therapy in such patients in whom a staphylococcal infection is suspected. (See Important Note below.)

Bacteriologic studies to determine the causative organisms and their sensitivity to nafcillin sodium should be performed.

In serious, life-threatening infections, oral preparations of the penicillinase-resistant penicillins should not be relied on for initial therapy.

Important Note: When it is judged necessary that treatment be initiated before definitive culture and sensitivity results are known, the choice of nafcillin sodium should take into consideration the fact that it has been shown to be effective only in the treatment of infections caused by pneumococci, Group A beta-hemolytic streptococci and penicillin G-resistant and penicillin G-sensitive staphylococci. If the bacteriology report later indicates the infection is due to an organism other than a penicillin G-resistant staphylococcus sensitive to nafcillin sodium, the physician is advised to continue therapy with a drug other than nafcillin sodium or any other penicillinase-resistant semi-synthetic penicillin.

Recent studies have reported that the percentage of staphylococcal isolates resistant to penicillin G outside the hospital is increasing, approximating the high percentage of resistant staphylococcal isolates found in the hospital. For this reason, it is recommended that a penicillinase-resistant penicillin be used as initial therapy for any suspected staphylococcal infection until culture and sensitivity results are known.

Methicillin is a compound that acts through a mechanism similar to that of nafcillin sodium against penicillin G-resistant staphylococci. Strains of staphylococci resistant to methicillin have existed in nature and it is known that the number of these strains reported has been increasing. Such strains of staphylococci have been capable of producing serious disease, in some instances resulting in fatality. Because of this there is concern that widespread use of the penicillinase-resistant penicillins may result in the appearance of an increasing number of staphylococcal strains which are resistant to these penicillins.

Methicillin-resistant strains are almost always resistant to all other penicillinase-resistant penicillins (cross resistance with cephalosporin derivatives also occurs frequently). Resistance to any penicillinase-resistant penicillin should be interpreted as evidence of clinical resistance to all, in spite of the fact that minor variations in **in vitro** sensitivity may be encountered when more than one penicillinase-resistant penicillin is tested against the same strain of staphylococcus.

Contraindications: A history of allergic reaction to any of the penicillins is a contraindication.

Warnings: Serious and occasionally fatal hypersensitivity (anaphylactoid) reactions have been reported in patients on penicillin therapy. Although anaphylaxis is more frequent following parenteral therapy it has occurred in patients on oral penicillins. These reactions are more apt to occur in individuals with a history of sensitivity to multiple allergens.

There have been reports of individuals with a history of penicillin hypersensitivity reactions who have experienced severe hypersensitivity reactions when treated with a cephalosporin. Before therapy with a penicillin, careful inquiry should be made concerning previous hypersensitivity reactions to penicillins, cephalosporins, and other allergens. If an allergic reaction occurs, appropriate therapy should be instituted, and discontinuation of nafcillin therapy considered. The usual agents (antihistamines, pressor amines, corticosteroids) should be readily available.

Precautions: As with any potent drug, periodic assessment of organ system function, including renal, hepatic and hematopoietic, should be made during prolonged therapy.

The possibility of bacterial and fungal overgrowth should be kept in mind during long-term therapy. If overgrowth of resistant organisms occurs, appropriate measures should be taken.

The oral route of administration should not be relied upon in patients with severe illness, or with nausea, vomiting, gastric dilatation, cardiospasm or intestinal hypermotility.

Safety for use in pregnancy has not been established.

Particular care should be taken with intravenous administration because of the possibility of thrombophlebitis.

Adverse Reactions: Reactions to nafcillin sodium have been infrequent and mild in nature. As with other penicillins, the possibility of an anaphylactic reaction or serum sickness-like reactions should be considered. A careful history should be taken. Patients with histories of hay fever, asthma, urticaria, or previous sensitivity to penicillin are more likely to react adversely.

The few reactions associated with the intramuscular use of nafcillin sodium have been skin rash, pruritus, and possible drug fever. As with other penicillins, reactions from oral use of the drug have included nausea, vomiting, diarrhea, urticaria, and pruritus.

Parenteral Administration: It is recommended that parenteral therapy be used initially in severe infections. The patient should be placed on oral therapy with this product as soon as the clinical condition warrants. Very severe infections may require very high doses.

Intravenous Route: The required amount of drug should be diluted in 15 to 30 ml. of Sterile Water for Injection, U.S.P., or Sodium Chloride Injection, U.S.P., and injected over a 5- to 10-minute period. This may be accomplished through the tubing of an intravenous infusion if desirable.

Stability studies on nafcillin sodium at concentrations of 2 mg/ml and 30 mg/ml in the following intravenous solutions indicate the drug will lose less than 10% activity at room temperature (70° F.) during the time period stipulated:

Isotonic sodium chloride	24 hours
5% dextrose in water	24 hours
5% dextrose in 0.4% sodium chloride solution	24 hours
Ringer's solution	24 hours
M/6 sodium lactate solution (conc. of 30 mg/ml)	24 hours

Discard any unused portions of intravenous solutions after 24 hours.

Only those solutions listed above should be used for the intravenous infusion of Unipen® (nafcillin sodium). The concentration of the antibiotic should fall within the range of 2 to 30 mg/ml. The drug concentrate and the rate and volume of the infusion should be adjusted so that the total dose of nafcillin is administered before the drug loses its stability in the solution in use.

There is no clinical experience available on the use of this agent in neonates or infants for this route of administration.

This route of administration should be used for relatively short-term therapy (24-48 hours) because of the occasional occurrence of thrombophlebitis, particularly in elderly patients.

Intramuscular Route: The clear solution should be administered by deep intragluteal injection immediately after reconstitution. After reconstitution, keep refrigerated (2°-8° C.) and use within 7 days or keep at room temperature (25° C.) and use within 3 days.

Oral Administration: Beta-hemolytic streptococcal infections should be treated for at least 10 days to prevent development of acute rheumatic fever or glomerulonephritis.

If oral therapy is inadequate, resort to parenteral nafcillin sodium.

After mixing, the oral solution must be stored in a refrigerator. Discard any unused portion after one week.

Supplied: INJECTION (VIALS)—Supplied in vial sizes of 500 mg., 1 gram, and 2 gram nafcillin sodium as the monohydrate, buffered. When reconstituted as recommended, the contents of each vial provides, respectively, 2-, 4- or 8-ml. of nafcillin sodium solution equivalent *per ml.* to 250 mg. nafcillin buffered with 10 mg. sodium citrate. Film-coated TABLETS—containing nafcillin sodium as the monohydrate, equivalent to 500 mg. nafcillin buffered with calcium carbonate. CAPSULES—containing nafcillin sodium, as the monohydrate, equivalent to 250 mg. nafcillin buffered with calcium carbonate. FOR ORAL SOLUTION—Combination pkg. of vial of dry nafcillin sodium as monohydrate and bottle of diluent—provides 80 ml. of solution containing equivalent of 250 mg. nafcillin per 5 ml. Alcohol 2%.

WYETH LABORATORIES PHILADELPHIA, PA.

Outpatient Management of Intercostal Tube Drainage in Spontaneous Pneumothorax

C. Mercier, M.D., A. Pagé, M.D., A. Verdant, M.D., R. Cossette, M.D.,
L. Dontigny, M.D., and L. C. Pelletier, M.D.

ABSTRACT **In a series of 226 patients with spontaneous pneumothorax, 167 (74%) were managed successfully on an outpatient basis by observation (20%) or by intercostal tube drainage and a flutter valve (54%). Only 59 patients (26%) were hospitalized, and 42 of these were treated surgically (18.6%). Outpatient management with a flutter valve has proved to be safe, efficient, and economical.**

A substantial increase in the incidence of spontaneous pneumothorax seen in our emergency ward led us to consider a new approach to its treatment. In 1973 we introduced intercostal tube drainage on an outpatient basis using a flutter valve.

Materials and Methods

During the 36-month period from January 1, 1973, to December 31, 1975, a consecutive series of 226 patients was treated for 274 episodes of spontaneous pneumothorax. The average follow-up period was 20.3 months. There were 169 male (75%) and 57 female (25%) patients. The mean age was 29 years, the youngest patient being 12 years of age and the oldest, 66 years. At their initial visit it was the first episode of spontaneous pneumothorax for 174 patients (77%), the second episode for 30 patients, and the third episode or more for the remaining 22 patients. Twenty-three patients (10%) had bilateral pneumothorax.

Outpatient Management

Patients with a lung collapse of 1 cm or less or an apical collapse of 4 cm or less were treated conservatively: after a short period of observation they were sent home, to be followed at the outpatient clinic.

When a more important pleural air space was present, intercostal tube drainage was instituted. Under local anesthesia a 16F catheter was inserted in the second intercostal space anteriorly in men and, for esthetic reasons, in the fifth intercostal space laterally in women. Underwater drainage was used temporarily. After an observation period of one to twelve hours a chest roentgenogram was obtained, and if the lung was adequately reexpanded, the underwater drainage was stopped and a disposable flutter valve (Heimlich, Bard-Parker; or Vycon, Belgium; Figure) was connected to the chest tube. The patient was then returned home. No antimicrobial drugs were given.

The patients with a chest tube and valve were seen at the outpatient clinic three or four days later. When lung expansion was complete and no air leak persisted, the tube was removed. Return to normal activity was permitted the following day.

In-Hospital Management

When incomplete lung reexpansion or an air leak persisted for seven days or more, the patient was hospitalized and underwater drainage with negative pressure was instituted. If, despite this treatment, the leak persisted for another week, an operation was considered.

Patients with multiple recurrences, a third episode on one side, or a second episode on the contralateral side were also hospitalized and operated upon. Other indications for in-hospital management were the presence of hemothorax or concomitant disease.

Results

Outpatient Management

Among the 49 patients initially managed conservatively, 45 healed without treatment and 1 required a chest tube and valve after the lung collapse was noted to have worsened; the remaining 3 patients were hospitalized.

One hundred sixty-nine patients were treated

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Presented at the Twelfth Annual Meeting of The Society of Thoracic Surgeons, Jan 26–28, 1976, Washington, DC.

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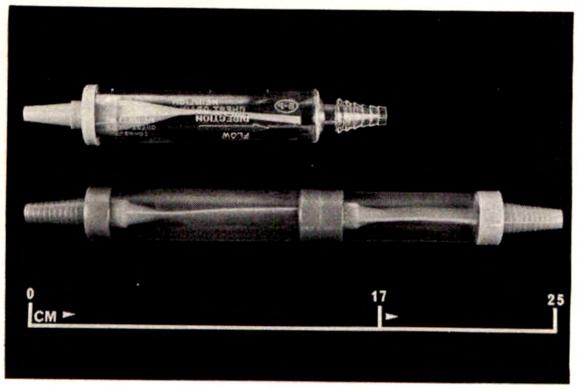

The disposable flutter valves: Heimlich (above) *and Vycon* (below).

with a chest tube and flutter valve. One hundred twenty-one healed completely without the need for further treatment. Thus, outpatient management was successful and definitive in 167 cases (74%) altogether (Table). Complete recovery was achieved with a total disability of less than a week in most cases. The length of drainage varied from 1 to 18 days with an average of 5.1 days. No complications resulted from this ambulatory treatment with the exception of a superficial wound infection in 1 patient.

In-Hospital Management

Fifty-nine patients (26%) were hospitalized. In 17, only underwater drainage with negative pressure was required. This group included 8 patients with persistent air leak, 4 with a moderate hemothorax, and 1 each with pneumonia, pulmonary insufficiency, silicosis, and fever of unknown origin. Another patient was hospitalized for a cesarean section.

Definitive Treatment of Spontaneous Pneumothorax in 226 Patients

Treatment	No. of Patients
Outpatient management	
Conservative	45
Chest tube & valve	122
Total	167 (74%)
In-hospital management	
Nonsurgical	17
Surgical	42
Total	59 (26%)

Forty-two patients (18.6% of the series) were treated surgically; hence 71% of the hospitalized patients were operated upon. The indications for operation were persistent air leak in 17 patients and multiple recurrences in 25. Thirty-one thoracotomies were performed in 30 patients, and 12 median sternotomies were done. There were no major complications. One patient had a minor recurrence five months after thoracotomy and was treated conservatively.

Comment

Two hundred seventy-four episodes of spontaneous pneumothorax were seen in a period of 36 months; this represents 0.1% of the patients admitted to our emergency ward in the same period of time. The incidence of spontaneous pneumothorax increased more than 100% compared with the rate before 1973. This is related to the regionalization of health care in the Province of Quebec, Canada.

This marked increase in the number of patients with spontaneous pneumothorax led us to reappraise our management of the condition in order to achieve better use of hospital facilities with a substantial saving in costs and without detriment to the quality of patient care. The result was this new approach of treating spontaneous pneumothorax on an outpatient basis. With a flutter valve, patients requiring tube thoracostomy did not necessarily need hospitalization. The use of a flutter valve is a safe, efficient, and reliable technique that is readily acceptable to patients. The device is quite inconspicuous under a loose garment and makes ambulatory treatment possible.

We have used either the Heimlich valve or the Vycon self-sucking chest drainage valve. The first is a single valve with a rigid outer casing. The other, with its second compartment, is a double self-sucking valve. It has a soft plastic casing that permits application of manual pressure in order to aspirate air or fluid. These valves are made of a latex rubber tubing that acts as a one-way valve to let air out and prevent its reentry. The Heimlich valve was used in most cases. We were equally satisfied with the Vycon valve, although it is bulkier and also noisier when an important air leak is present.

With increasing experience in this form of treatment, the initial underwater drainage period was often eliminated and the valve was applied directly to the chest tube. Thus the observation period could be reduced to less than an hour. Some of our patients resumed normal activity with a chest tube and valve in place.

When surgical treatment is needed, a limited axillary thoracotomy through the fourth intercostal space has become the preferred approach. This is as adequate, less traumatic, and more cosmetic than a median sternotomy. The blebs were usually sutured at their base with a surgical stapler and left in place. Occasionally they were resected. Dry-sponge abrasion of the parietal pleura was also performed to promote adhesions. We do not support the use of pleurectomy as a routine procedure except in rare instances of disseminated blebs.

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Discussion

DR. PAUL A. THOMAS (Chicago, IL): I congratulate the authors on their progressive approach to this fairly common problem in an unusually large series of patients.

As you are all aware, a number of innovative valving devices have been applied to chest tubes for this same purpose, and I would like to discuss a flap valve of our own design. We reported on the use of this valve for similar purposes in a series of patients in 1957.

The assembled device is a plastic-encased flap valve that one attaches to the chest tube. Although our patients were hospitalized, they were treated on a completely ambulatory basis. After the chest tube is inserted, the valve is attached to it and taped to the chest wall. The patients are able to move about the hospital ward and conduct their own affairs, as illustrated by the authors in their outpatient treatment program.

DR. HENRY J. HEIMLICH (Cincinnati, OH): Dr. Mercier and his coauthors are to be congratulated on developing a safe method for treating pneumothorax and for reducing hospitalization costs, an unusual step these days.

Several hundred thousand Heimlich chest drainage valves have been used since they were first developed ten years ago, and no major difficulties have been reported. As a result of the hundreds of lives the valves are credited with saving in the wars in Vietnam and Israel, they have become recognized as an emergency item. Their primary use, however, continues to be in elective thoracic operations.

Postoperatively, a valve is connected to each chest tube and drains into a urinary drainage bag. This arrangement permits the function of each tube to be observed individually. Immediate ambulation is possible, and transporting the patient to the radiology department enables lateral as well as posteroanterior films to be taken. Of equal importance is the security that results from the ease with which the valve's function can be understood by the nursing staff, who are frequently overwhelmed by the complexity of suction apparatus.

The valve enables the pleural cavity to be evacuated without the encumbrance of suction, because the expansion of the lung itself—either by positive pressure through the endotracheal tube or by postoperative coughing—forces air and fluid out of the chest, and they are prevented from returning to the pleural cavity when a valve is in the drainage system.

Suction apparatus attached to chest tubes is generally unnecessary except in selected cases, as described by Dr. Mercier. Underwater suction drainage not only is expensive and confines the patient to bed, but it can be dangerous. Suction on a chest tube, for example, can draw air through an intrathoracic esophagogastric anastomosis and result in a fistula with leakage into the pleural cavity.

The Incidence of Venous Thrombosis Following Long-Term Transvenous Pacing

William S. Stoney, M.D., Ronald B. Addlestone, M.D.,
William C. Alford, Jr., M.D., George R. Burrus, M.D.,
Robert A. Frist, M.D., and Clarence S. Thomas, Jr., M.D.

ABSTRACT **Long-term cardiac pacing with permanent transvenous electrodes has achieved wide acceptance with only occasional reports of venous obstruction and edema. To determine the incidence of venous abnormalities associated with transvenous electrodes, 34 venograms were obtained in 32 patients paced 18 months or longer. Eleven venograms demonstrated severe obstruction with collateral circulation communicating with the opposite cervical and innominate venous channels; 7 of these showed total occlusion. Seven venograms revealed no obstruction. The remaining 16 venograms showed venous stenosis without collaterals.**

It is concluded that venous abnormalities associated with permanent transvenous pacing occur commonly but are not usually associated with arm or facial edema.

Permanent cardiac pacing utilizing transvenous electrodes has become one of the most satisfactory cardiac surgical procedures developed in the past fifteen years. Although initially permanent pacemakers were associated with frequent problems and failure related to the electrodes and components, the units available at present are noted for reliability and durability.

Complications produced by electrode fracture and displacement, late threshold elevation, and premature battery failure still occasionally occur but have been diminished by improvements in electrode and pacemaker design and in surgical technique. Venous thrombosis of the subclavian or innominate vein containing the permanent electrode has been infrequently described. The actual incidence of venous abnormalities associated with permanent transvenous pacemaker electrodes has been reported [1, 7] but has received little attention in the English literature. To assess the frequency of venous abnormalities produced by pacemaker electrodes, a group of patients was evaluated by venography.

Materials and Methods

During a 6-month period, subclavian venograms were obtained in patients with permanent pacemakers who were hospitalized for elective replacement. All electrodes had been functioning for two years or more except 1 which had been in place for 18 months. All patients admitted for pacemaker replacement were studied except those excluded by request of the patient or the referring physician. The permanent pacemaker electrode had been inserted in the external jugular vein in a few patients, but the majority had been placed in the cephalic vein at the deltoid-pectoral junction.

Thirty-two patients were studied. Two patients had had an electrode in each subclavian vein in the past, and bilateral venograms were obtained. A total of 34 venograms was available for study.

The venograms were performed by placing a 16-gauge cannula in a peripheral arm vein on the side to be studied. Using forceful hand injection, 50 cc of Conray-60 was injected and ten films were exposed at a rate of one frame per second. In 3 patients bilateral simultaneous injections were made.

Results

A normal venogram with no obstruction was found in only 7 patients (21%) (Fig 1). Mild obstruction estimated to be less than 50% of the lumen of the innominate or subclavian vein was found in 5 additional patients (15%). Obstruc-

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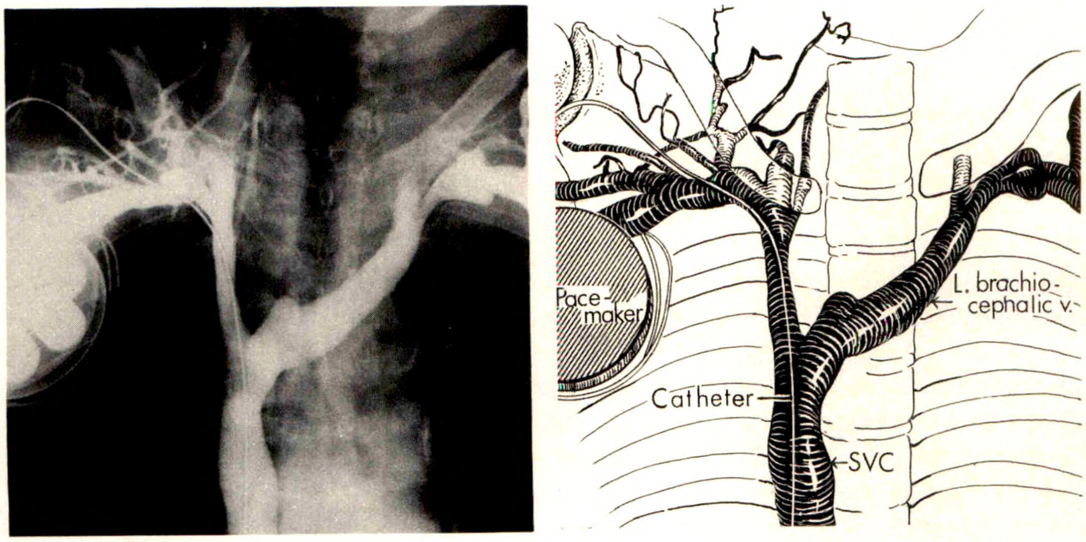


Fig 1. A normal venous system containing a bipolar electrode. (SVC = *superior vena cava.)*

tion involving 50 to 90% of the lumen was seen in 15 patients (44%) (Fig 2); 4 of them had cervical collateral venous channels. In 7 patients (21%) total venous obstruction was observed (Fig 3); each of these patients had well-developed venous collateral circulation.

A small unipolar Cordis or Starr-Edwards electrode had been utilized in 11 patients, and although partial occlusion was frequently observed, only 1 patient with a unipolar electrode had total venous obstruction. The remaining 23 electrodes were bipolar Medtronic units, and 6 of them were associated with complete occlusion. This suggests that a large bipolar electrode is more likely to produce obstruction than a smaller unipolar electrode.

The obstruction was commonly located in the central part of the subclavian vein 2 or 3 cm proximal to the cephalic vein, which was the usual site of cannulation. In 7 patients the obstruction was noted in the innominate vein at its junction with the superior vena cava. In no instance was the superior vena cava involved.

Clinical symptoms and physical findings were rare. One patient was hospitalized because of sudden onset of pain and edema of the left arm after four years of uneventful cardiac pacing. A venogram revealed complete obstruction of the innominate and subclavian veins extending out to the axillary vein (Fig 4). Following initial arm elevation and intravenous heparinization the acute symptoms subsided, and 3

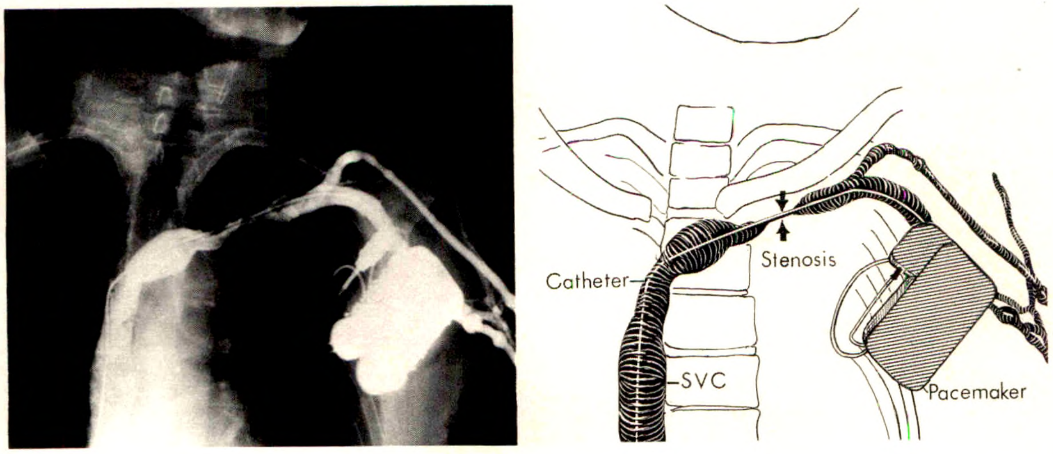


Fig 2. Severe stenosis of the subclavian vein, which contains a unipolar electrode. There are no collaterals. (SVC = *superior vena cava.)*

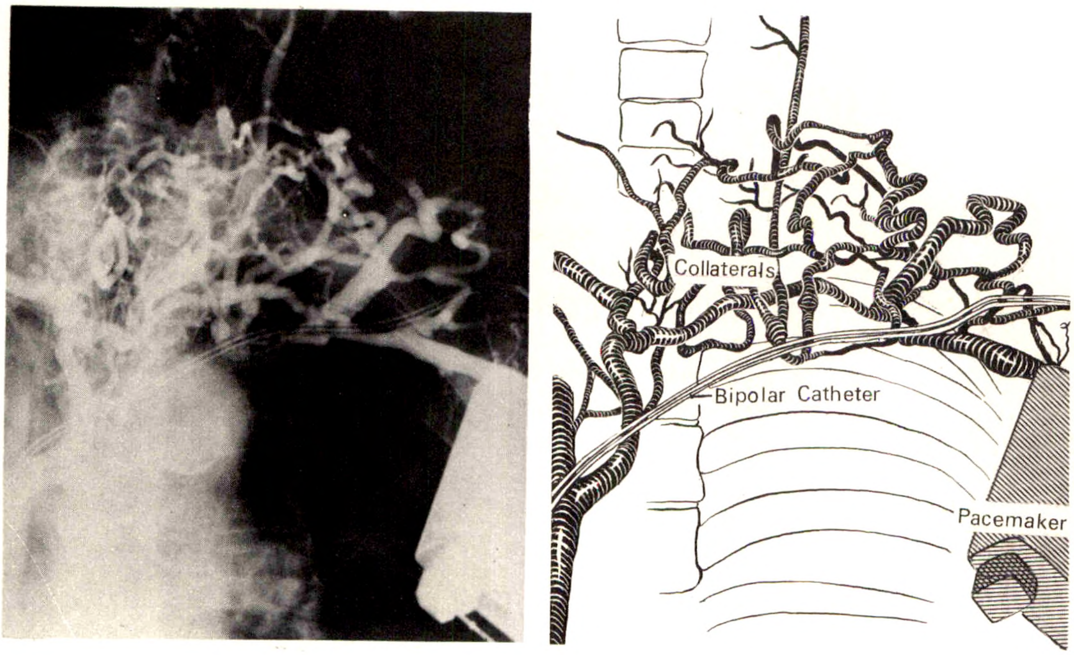


Fig 3. Total venous obstruction of the innominate and subclavian vein with elaborate cervical collaterals.

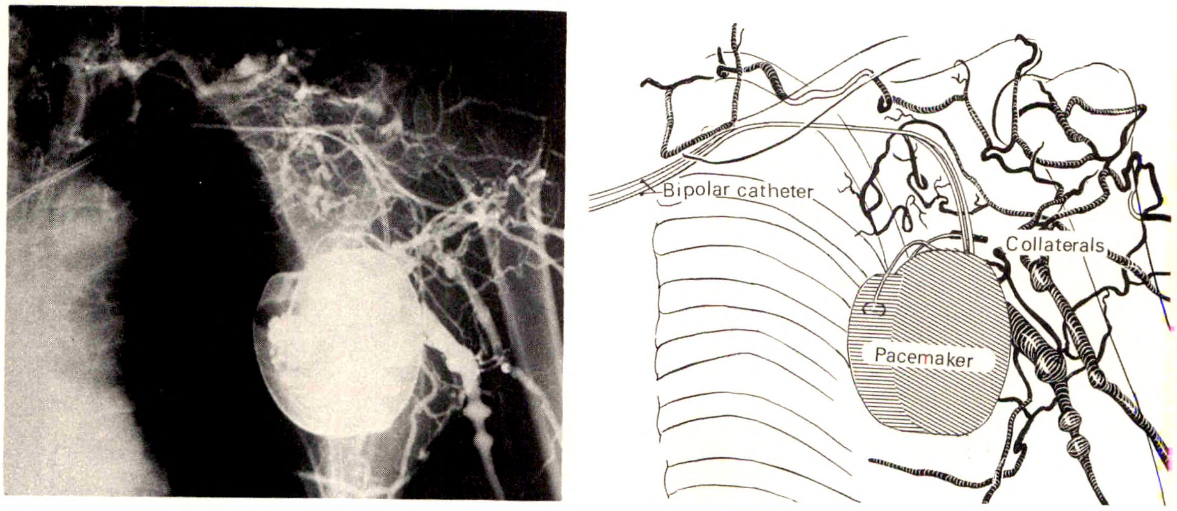
months later the arm had returned to normal size. Several patients were noted to have either a prominent external jugular vein or a conspicuous subcutaneous venous pattern in the pectoral region, and this was usually associated with an abnormal venogram. Other than minimal dependent edema of the hand, the remaining patients were asymptomatic.

One additional physical sign of jugular venous obstruction has been observed during examination of the supine patient. The absence of a venous pulse in the internal jugular vein on the same side as the pacemaker and electrode, with a prominent cardiac venous pulse in the contralateral jugular system, is suggestive of occlusion on the nonpulsatile side. This physical sign has been observed and confirmed by venography in a single patient and suggests that examination of each jugular system by Doppler ultrasonography could identify venous obstruction without venography.

Comment

One of the initial objections to the concept of permanent transvenous cardiac pacing was the

Fig 4. Total subclavian venous obstruction extending back to the axillary vein with few cervical collaterals. This patient had severe arm edema.



prediction that a significant number of patients would develop thrombosis of the superior vena cava or innominate vein. This prediction was based on the rather frequent occurrence of venous thrombosis associated with central venous catheters introduced through a peripheral vein and the incidence of venous thrombosis following placement of ventriculovenous shunts for hydrocephalus [8]. Surprisingly, venous thrombosis has not been a common problem with long-term transvenous pacing. Only 4 cases of symptomatic superior vena caval obstruction have been documented [5, 10–12], and 4 additional reports have been published describing axillary-innominate venous obstruction associated with permanent transvenous electrodes [2–4, 9]. All these patients had sudden onset of edema of the face or arm, and the venous obstruction was documented by venography.

On the other hand, two recent reports in the German literature suggest that venous obstruction associated with permanent pacemaker electrodes is more common than has previously been suspected. Balau, Marx, and colleagues [1] obtained venograms in 49 patients who were hospitalized for elective pacemaker replacement and found evidence of innominate and subclavian thrombosis in 14. Six patients had extensive collateral circulation in the region of the obstruction, and 3 had chronic edema of the arm. A year later they reported the findings from venograms in 120 patients with permanent transvenous pacemakers [7]; the venograms were obtained both early (10 to 30 days) and late (6 to 36 months). Evidence of venous thrombosis was discovered in 34 patients, 18 of whom had collateral venous circulation at the site of obstruction. Six patients had edema of the arm, 4 of these in the first 30 days after pacemaker implantation. In our study a similar ratio of patients was observed to have abnormalities of the venous system containing the permanent pacemaker electrode (Table).

Although venous abnormalities associated with permanent pacemaker electrodes are far more common than previously suspected, only an occasional patient has been noted to have facial or arm edema. It is possible that innominate and subclavian obstruction occurs gradually, allowing an adequate collateral circulation to develop so that edema is unusual. Sudden thrombosis in the first few weeks after implantation would be more likely to produce edema since collaterals would not have formed. Similarly, extension of a previously localized obstruction into the axillary vein could obliterate collaterals and produce late symptoms. It was suspected that our single symptomatic patient may have had such progression of thrombosis.

Pulmonary embolism has been observed as a rare complication of both temporary and permanent transvenous electrodes [6]. In the majority of reported cases the embolus originated in the right atrium or right ventricle. The innominate-subclavian system should also be closely evaluated as a possible source if pulmonary embolization occurs in a patient with a temporary or permanent pacemaker.

If a permanent pacing catheter fails and the same site is to be used for replacement, a preliminary venogram should be considered since complete or partial stenosis of the innominate-subclavian drainage is likely. In 1 of our patients venography showed both innominate veins to be completely occluded; successful pacing was reestablished utilizing myocardial electrodes.

Reports of Venograms in Patients with Permanent Pacemaker Electrodes, Excluding Single Case Reports

Report	No. of Venograms	No. Abnormal	Venous Obstruction with Collaterals	Arm or Facial Edema
Balau et al [1]	49	14 (29%)	6 (12%)	3 (6%)
Marx et al [7]	120	34 (28%)	18 (15%)	6 (5%)
This report	34	15 (44%)	7 (21%)	1 (3%)
Total	203	63 (31%)	31 (15%)	10 (5%)

These findings lead to the conclusion that occult venous obstruction occurs in a significant number of patients with transvenous electrodes. This may have therapeutic implications should pulmonary embolization occur, and it may also affect surgical management if a catheter requires removal with replacement through the same innominate venous system.

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Discussion

DR. SEYMOUR FURMAN (Bronx, NY): A review of our patients shows 5 who have had some kind of symptomatic thrombophlebitis or edema of the arm on the side of implantation out of approximately 1,600 patients who have received a transvenous cardiac pacemaker. One patient was quickly found to have an associated carcinoma of the pancreas. No abnormality was discovered in the second, and the edema receded spontaneously within approximately ten days. The remaining 3 had immediate postimplantation edema; in 2 it receded promptly, but in the third it has persisted at a very mild level for more than a year and has necessitated specific therapy.

While the occurrence of embolization from this site should call attention to the possible thoracic venous origin of pulmonary emboli, so few instances of pulmonary embolism have been reported in the medical literature that it remains an unusual complication of transvenous pacer therapy. Perhaps the most significant finding of Dr. Stoney's report, our review of our own patients, and the descriptions in the literature is the benign and even asymptomatic nature of what seems to be radiologically significant venous thrombosis. Three patients with partially or totally occluded venous systems were detected only during investigation and were totally asymptomatic, indicating that the thrombosed vein is a far less significant lesion than the roentgenogram suggests.

DR. STONEY: I thank Dr. Furman for his remarks. I believe he has summarized the essence of this discussion: that although venous abnormalities occur frequently, they are almost never a clinical problem.

Our findings are not intended in any way to denigrate the transvenous electrode as a primary technique in cardiac pacing, and of course we use it as our technique of choice.

Human Heart Transplantation: Current Status

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Charles P. Bieber, M.D., Bruce A. Reitz, M.D., Jack G. Copeland, M.D.,
Philip E. Oyer, M.D., and Norman E. Shumway, M.D.

ABSTRACT **The overall survival rate for 97 heart transplant recipients operated on from 1968 to 1975 has been 49% at one year and 23% at five years. Progressive improvement in one-year survival has been achieved, from 22% in 1968 to 62% in 1974. The major factors responsible for increasing survival are better understanding and management of acute and chronic rejection. Current results suggest that heart transplantation deserves wider application in the treatment of selected patients with end-stage myocardial insufficiency.**

Considerable interest in cardiac transplantation has been maintained in our institution since 1968 and had resulted in the performance of 102 transplants in 97 patients by the end of 1975. The clinical experience accumulated in caring for these patients, coupled with input from studies carried out in the animal laboratory, has led to a progressive increase in patient survival and rehabilitation. Within the last few years, several important advances have been made in the treatment of acute and chronic rejection. This communication deals chiefly with the management of these two entities.

Acute Rejection

Maintenance Immunosuppression

Azathioprine and corticosteroids remain the primary agents for maintenance immunosuppression following heart transplantation. An azathioprine loading dose of 5 mg per kilogram of body weight is given immediately preoperatively. Maintenance azathioprine is begun postoperatively as soon as the patient is able to take oral medications and is continued indefinitely at the highest dose compatible with adequate marrow function, usually 2 to 3 mg/kg daily. Corticosteroid therapy consists of intravenous methylprednisolone, initially administered intraoperatively and then continued for 48 hours following operation. Subsequently oral prednisone is administered, beginning with 1.5 mg/kg daily, then tapering to 1 mg/kg by two months postoperatively and to 0.5 mg/kg by six months. Thereafter, a continual effort is made to decrease prednisone to the lowest dose compatible with satisfactory allograft function. Long-term maintenance doses average 0.4 mg/kg daily. Intramuscular rabbit anti-human-thymocyte globulin (RATG) is begun immediately after the operation and continued for the first ten postoperative days.

Diagnosis

Electrocardiographic evaluation and cardiac auscultation remain the two most important clinical surveillance techniques for detecting an acute rejection crisis [5]. Electrocardiographic correlates of rejection consist of an overall decrease in QRS voltage, the appearance of arrhythmias (usually atrial in origin), and in some instances a rightward shift of the mean QRS vector. At the time of operation an epicardial lead is attached to the donor atrium, and a decrease in the QRS voltage recorded from this lead may be the harbinger of an acute rejection crisis.

The most useful physical finding in diagnosing an acute rejection crisis is the appearance of a ventricular filling sound, most frequently an S_3 gallop. In the absence of acute rejection injury, gallop sounds are not characteristic of the human heart transplant, and the intensity of the gallop sound during an acute rejection crisis serves as a useful indicator of the severity of rejection.

Endomyocardial biopsy has substantially in-

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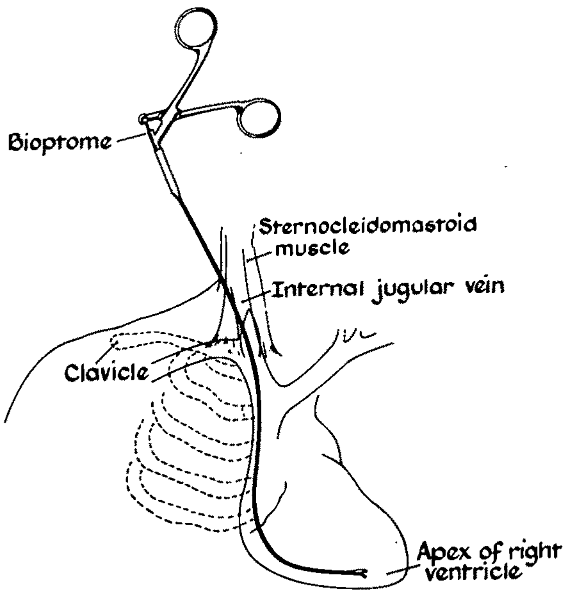
creased the certainty with which the diagnosis of acute rejection can be made and also provides objective evidence of the efficacy of antirejection therapy [3]. Cardiac biopsy is performed under local anesthesia by introducing a biopsy forceps into the internal jugular vein using a modified Seldinger technique. Under fluoroscopic control the biopsy forceps is guided into the right ventricle, and a 1 × 3 mm specimen of myocardium is removed from the intraventricular septum (Fig 1). Sufficient tissue can usually be obtained for staining with hematoxylin and eosin and with methylpyronine green. When it is important to determine the presence of rejection on an emergency basis, frozen sections have been helpful.

To date, 470 endomyocardial biopsies have been performed in recipients of cardiac transplants. Satisfactory tissue for diagnosis has been obtained in more than 95% of these biopsies. Complications have been relatively minor and consisted of premature ventricular contractions in approximately 20%, supraventricular arrhythmias in 3%, and pneumothorax caused by trauma to the apical pleura during introduction of the biopsy forceps in 2%.

Using a combination of clinical and histological findings, it has been possible to standardize the diagnosis and management of acute rejection. A drop of 20% or more in the QRS voltage (from either the standard electrocardiographic leads or the atrial wire), the development of a new arrhythmia, or the appearance of a gallop sound are considered presumptive evidence of acute rejection injury, and an endomyocardial biopsy is obtained within several hours. If the clinical findings argue strongly for the presence of acute rejection or if there is reason to believe that the presumptive episode is likely to be a severe one, antirejection therapy is begun immediately after obtaining the biopsy. If the clinical findings are equivocal, therapy is delayed for approximately twelve hours until permanent histological sections can be obtained. Antirejection therapy involves increasing the dosage of corticosteroids, and occasionally RATG, and beginning administration of actinomycin D and heparin. The complete treatment regimen consists of the following:

1. Methylprednisolone, 1.0 gm IV daily for 2 to 4 days.
2. Actinomycin D, 200 μg IV daily for 1 to 3 days.
3. Antithymocyte globulin IM for 3 to 5 days.
4. Prednisone increased for 10 to 14 days.
5. Heparin IV for 5 to 7 days.

Fig 1. Technique of endomyocardial biopsy.



Rabbit Antithymocyte Globulin (RATG)

During the first two years following the inception of clinical cardiac transplantation we used heterologous antisera produced from horses, against either thoracic duct lymphocytes or splenocytes, as an immunosuppressive adjunct. Subsequently we found horse anti-human-thymocyte globulin (HATG) to be somewhat more efficacious than the earlier preparations [6]. In late 1973 we made a further change and began using antithymocyte globulin raised in rabbits. The procedures for immunization and harvesting of the rabbit antiserum are similar to the protocol used by Davis and colleagues [4]. The purified globulin fraction is administered intramuscularly in a dose of 3 to 15 mg/kg on postoperative days 1, 2, 3, 5, 7, and 9. Doses of individual batches are adjusted on the basis of the sheep red blood cell rosette inhibition titers. Serum levels of rabbit globulin in the cardiac recipients are assayed serially utilizing a modified Farr technique [1].

Table 1. Comparison of the Efficacy of RATG and HATG in Preventing Rejection

Factor[a]	RATG	HATG	p Value
Rejection onset	23.8 ± 0.5	12.6 ± 0.5	0.01
Rejection frequency	2.9 ± 0.07	5.0 ± 0.1	0.002
Rejection score	4.7 ± 0.6	7.5 ± 0.3	0.05

[a] Rejection onset is the postoperative day on which the first rejection crisis is diagnosed. Rejection frequency is the number of rejection episodes per 100 patient-days occurring in the first two postoperative months. Rejection score is computed similarly to rejection frequency except that each episode is graded mild, moderate, or severe and weighted accordingly in the calculation of score. Mean values are shown with standard errors.

Factors indicative of rejection in the first 29 patients receiving RATG were compared with those in the last 20 patients receiving HATG. In all patients, episodes of acute rejection were confirmed by cardiac biopsy. As shown in Table 1, by each of the three variables assayed, rejection was significantly less severe in patients who were given RATG than in those receiving HATG.

Serial determination of rabbit globulin levels allowed the patients receiving RATG to be divided into two distinct groups as determined by the kinetics of rabbit globulin elimination from the serum. In 19 patients rabbit globulin was rapidly eliminated, with a mean half life of 1.4 ± 0.4 days. In 10 patients the serum rabbit globulin half-life was prolonged, with values ranging from 4 to 18 days and averaging 9.0 ± 4.3 days. Table 2 compares rejection indicators in these two groups of patients. It is readily apparent that in patients in whom rabbit globulin was eliminated in a slow and presumably nonimmune fashion, the incidence and severity of acute rejection were substantially diminished. Thus it is apparent not only that RATG is a more potent immunosuppressive agent than HATG, but also that more effective immunosuppression is obtained in patients in whom RATG is not subject to immune elimination.

Table 2. Comparison of Rejection in Patients with Rapid versus Slow RATG Clearance from the Serum

Factor[a]	Slow Elimination	Rapid Elimination	p Value
Rejection onset	32.3 ± 1.7	19.3 ± 0.6	0.001
Rejection frequency	1.9 ± 0.1	3.9 ± 0.2	0.001
Rejection score	2.5 ± 0.2	5.8 ± 0.3	0.001

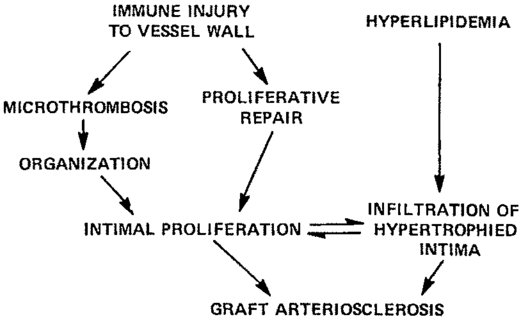
[a] See Table 1 for explanation.

Chronic Rejection

Although survival immediately following transplantation depends upon the management of acute rejection episodes and infections, it became apparent relatively early in our experience that the major determinant of long-term survival of the cardiac allograft recipient was development of arteriosclerosis in the transplanted heart. Our first long-term survivor died at twenty-one months of an acute myocardial infarction, and extensive coronary artery lesions were evident at postmortem examination. Similar findings were present postmortem in Barnard's first long-term survivor [10]. Based on the histological appearance of the lesions and the rapidity with which they developed, a tentative hypothesis for the pathogenesis of graft arteriosclerosis was formulated. It seems probable that the initial event is immune injury to the tunica intima of the coronary vessel, resulting in endothelial slough and exposure of a thrombogenic surface. Microthrombi, consisting predominantly of platelets, accumulate and undergo organization, forming a small intimal lesion. Repetition of this process, compounded by the infiltration of plasma lipids into the hypertrophied tunica intima, which elicits additional inflammation, results in continuous formation of intimal lesions and consequent luminal narrowing. A schema of the proposed pathogenic mechanism is shown in Figure 2.

On the basis of this hypothesis and studies performed by Kincaid-Smith [9] in renal allo-

Fig 2. Proposed pathogenesis of graft arteriosclerosis.

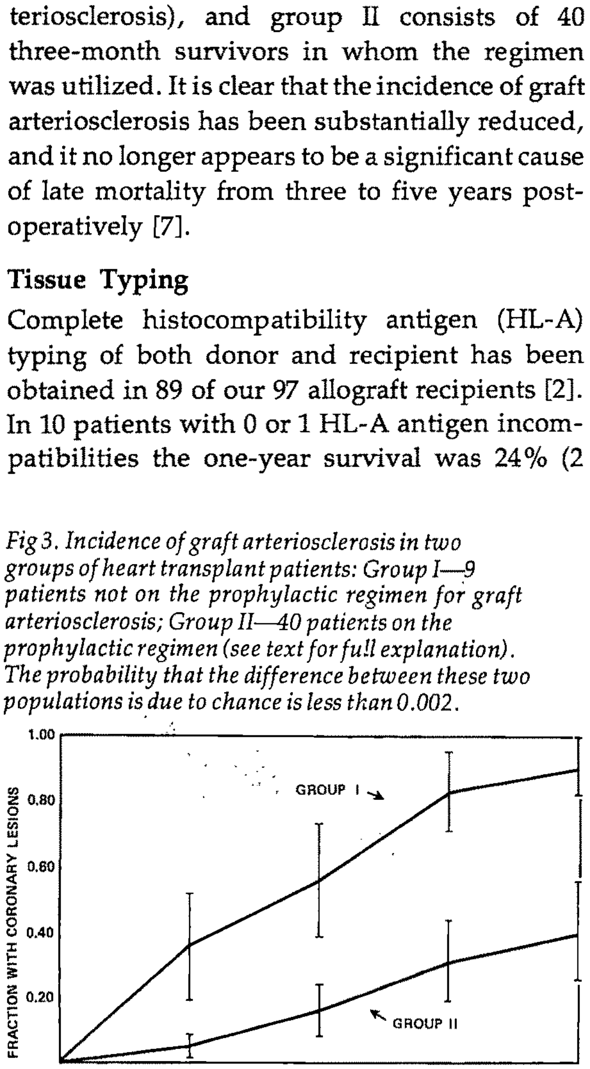


graft recipients, we thought that a combination of antithrombotic therapy and a sustained attempt to lower plasma lipid levels might be effective in reducing the severity of graft arteriosclerosis. Accordingly, after January, 1970, all patients receiving cardiac allografts were placed on a continuous regimen of warfarin and dipyridamole following transplantation and were given a diet low in cholesterol and saturated fat, with calorie restriction designed to maintain normal body weight. The incidence of graft arteriosclerosis has subsequently been assayed by annual coronary arteriography or postmortem examination [8]. Figure 3 depicts the time-related incidence of graft arteriosclerosis in all patients in our series who have survived beyond three months. Group I consists of 9 three-month survivors operated on prior to 1970 (before initiation of the regimen designed to prevent graft arteriosclerosis), and group II consists of 40 three-month survivors in whom the regimen was utilized. It is clear that the incidence of graft arteriosclerosis has been substantially reduced, and it no longer appears to be a significant cause of late mortality from three to five years postoperatively [7].

Tissue Typing

Complete histocompatibility antigen (HL-A) typing of both donor and recipient has been obtained in 89 of our 97 allograft recipients [2]. In 10 patients with 0 or 1 HL-A antigen incompatibilities the one-year survival was 24% (2 patients); in 19 patients with 2 mismatches it was 53% (10 patients); in 37 patients with 3 mismatches, 48% (18 patients); and in 23 patients with 4 mismatches, 55% (13 patients). No significant differences in survival have occurred between any of the groups, and in addition, no correlation between the number of HL-A mismatches and history of rejection has been evident. In the last two years one of us has devised a technique for calculating match score in which specific HL-A incompatibilities are weighted by the frequency with which antibodies are formed during pregnancy in the face of known maternal-offspring HL-A incompatibilities. Utilizing this statistic, a significant correlation emerges between match score and survival [7]. At present, however, this correlation does not appear strong enough to justify using match score to determine suitable cardiac donors preoperatively.

Fig 3. Incidence of graft arteriosclerosis in two groups of heart transplant patients: Group I—9 patients not on the prophylactic regimen for graft arteriosclerosis; Group II—40 patients on the prophylactic regimen (see text for full explanation). The probability that the difference between these two populations is due to chance is less than 0.002.



Retransplantation

Cardiac retransplantation has been carried out 5 times in our series. In 1 patient successful retransplantation was accomplished 24 hours following placement of the initial graft, which had an extremely unstable rhythm with resultant compromise of hemodynamic function. In 2 patients retransplantation was carried out during the first two postoperative months because of unremitting, drug-resistant, acute rejection injury. In 1 of these patients the second graft was rejected within two weeks, but acute rejection in the other patient was relatively easy to control and the patient is at present a long-term survivor. Cardiac retransplantation was required in 2 patients because of the development of severe coronary artery lesions in the original graft after two to five years. One of them died postoperatively of a fungal infection that had been present at the time of retransplantation. The second patient continued to do well more than one year following placement of his second graft.

Survival and Rehabilitation

Figure 4 depicts the survival curve of the 97 patients who have received heart transplants. The majority of deaths occurred within the first year following transplantation, so that if an individual reaches his first anniversary, he has approximately a 50% chance of continuing to

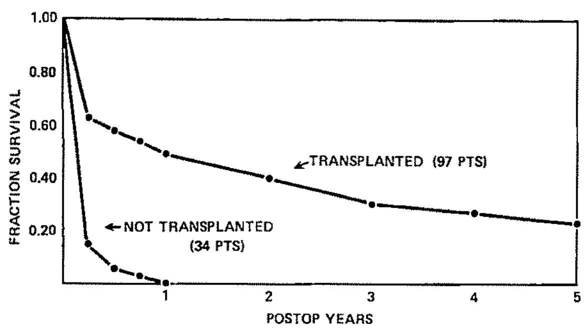


Fig 4. Survival of 97 patients who received heart transplants and 34 patients selected for transplantation who died before a donor became available.

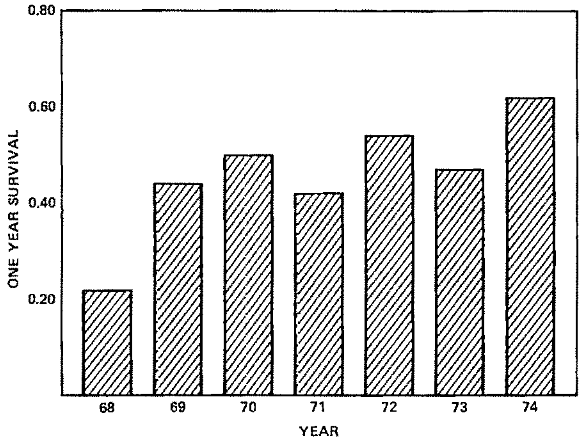


Fig 5. One-year survival by calendar year in the Stanford University series.

survive for five years following operation. Also shown in Figure 4 is the survival curve for 34 patients who were selected for transplantation but who died before a suitable donor became available; all had died by one year following selection. Figure 5 depicts one-year survival by calendar year from 1968 through 1974, the last year in which a complete one-year survival can be ascertained. Progressive improvement in one-year survival is apparent; 1974 one-year survival was 62%. The statistics for rehabilitation, which is as important as survival, are equally encouraging. Of the 37 patients in our series who have survived for one year or more, 32 (86%) have been rehabilitated to New York Heart Association Functional Class I.

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Discussion

DR. GRIEPP: It is always a pleasure to present these data, but sometimes I wonder whether a paper on heart transplantation is accepted on its merits or because it saves time during the discussion period.

I should like to present some additional information as an encouragement to others contemplating initiation of a program in heart transplantation. We have plotted the cost of heart transplantation over the years compared with the cost of aortic valve replacement in our hospital. In 1970 the average cost of heart transplantation was about $20,000, approximately six times the cost of an aortic valve replacement. In the past year the average cost of a heart transplant was just under $30,000, but this now represents only four times the cost of aortic valve replacement. Thus, the cost of heart transplantation is decreasing in comparison to more standard types of cardiac operations.

With respect to long-term survival and rehabilitation, 5 patients have currently lived beyond five years. Our longest survivor is a man who is alive and active more than six years following operation. Most of our long-term survivors are doing quite well and leading close to normal lives. More than 85% of the one-year survivors are in New York Heart Association Functional Class I, and of these patients, greater than 80% have returned to gainful employment.

Cardiac Performance and Oxygen Consumption during Intracardiac Operations in Children

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ABSTRACT **Cardiac performance and oxygen consumption in 30 patients undergoing surgical treatment for congenital cardiac disease were determined from intraoperative measurements. Arterial pressure, cardiac index, mean left ventricular hydraulic output power, and pulmonary artery oxygen saturation were obtained at average mean left atrial pressures of 8.1 and 15.2 cm H_2O after cardiopulmonary bypass in 20 patients. These same variables were measured at an average pulmonary artery saturation of 65 and 75% in 30 patients. A composite of measurements of cardiac performance was desirable to guide precise patient care intraoperatively, especially if myocardial function was compromised. It is suggested that left atrial pressure be maintained at a level that results in a pulmonary artery saturation greater than 65%.**

The significant decrease in immediate mortality [7] and morbidity after open-heart operations for congenital cardiac disease can be attributed to improved techniques of intracardiac surgery, cardiopulmonary bypass, and myocardial protection during bypass [3, 4]. Thus, the postoperative course frequently is uneventful if a surgical procedure has significantly reduced atrial and ventricular inflow and outflow gradients, abolished intracardiac shunts, preserved the coronary circulation, and maintained an appropriate heart rate. However, it is not unusual to see compromised cardiac performance in the immediate postoperative period, frequently manifested by hypotension, decreased urinary output, and cool skin. Since blood transfusion is frequently employed to treat this situation, we evaluated the effects of increasing left atrial pressure (preload) on cardiovascular performance [7] immediately following completion of cardiopulmonary bypass for surgical repair of congenital cardiac defects.

Methods

Thirty individuals were selected from the routine sequence of patients undergoing surgical treatment for congenital cardiac disease necessitating cardiopulmonary bypass. The patients ranged in age from 1 to 18 years and in weight from 8.6 to 66.5 kg. Of these patients 9 had an atrial septal defect, 8 a ventricular septal defect, 2 pulmonic stenosis, 6 aortic stenosis, 3 tetralogy of Fallot with preexisting surgically created shunts, and 2 transposition of the great arteries.

Prior to bypass a central venous pressure line was inserted, and the radial artery was cannulated for arterial pressure determinations. All patients were artificially ventilated during the operation. The chest was opened by a median sternotomy. The aorta and venae cavae were isolated, and an electromagnetic flow probe of appropriate size was placed around the root of the aorta in 10 of these patients. This probe measures forward blood flow but excludes coronary flow. Electrical signals of arterial pressure from a P23 Db transducer* and of aortic blood flow from a K4000 flowmeter* were displayed on an oscilloscope for inspection, and a digital readout of mean values was obtained.

Mean left ventricular hydraulic output power (MLVP) was calculated electronically in gram-meters per minute by the equation:

$$\text{MLVP} = \frac{1}{N} \int_{0}^{N} \text{Pa} \times \text{Qa dt}$$

where Pa = instantaneous arterial pressure, Qa = instantaneous aortic blood flow, t = time,

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and N = interval in time from R wave to R wave: Mean MLVP was displayed on a digital meter as well as recorded. Mean systemic vascular resistance was calculated electronically (Motorola MC1494) by dividing mean arterial pressure by mean aortic blood flow and was displayed on a digital meter and recorded. Cardiac output was also displayed digitally and recorded.

After the completion of flow, resistance, power, central venous pressure, and arterial pressure measurements, the flow probe was removed and the aorta and cavae were cannulated for perfusion. Just prior to discontinuing bypass a catheter was advanced through the chest wall and inserted into the left atrium, then connected to a water manometer for direct readout of left atrial pressure (LAP). After bypass was stopped, the aortic cannula used for perfusion was withdrawn and the aortotomy was closed. An electromagnetic flow probe was again placed around the root of the ascending aorta. The cardiac defects were repaired during cardiopulmonary bypass at 31° or 37°C.

A 6F catheter was inserted through the muscle of the right ventricular outflow tract and advanced into the pulmonary artery. After right ventricular and pulmonary artery pressures were recorded, blood samples were withdrawn from the pulmonary artery for measurement of oxygen saturation using an AO oximeter.*

Oxygenated blood was transfused into the right atrium from the heart-lung pump to elevate LAP serially from approximately 5 to 20 cm H_2O. During incremental transfusion of blood, the following were obtained: central venous pressure, LAP, arterial pressure, left ventricular power, systemic vascular resistance, cardiac output, and systemic arterial and pulmonary artery oxygen saturations. Cardiac output and MLVP were converted to indices based on square meters of body surface area. Oxygen consumption was calculated from the Fick equation using cardiac output from the electromagnetic flowmeter and the arteriovenous oxygen saturation difference in volumes percent.

These studies were performed with the chest open at 37°C while the surgeon was achieving hemostasis. Only 5 to 10 minutes were required to accomplish these measurements after perfusion.

Two groups of patients were identified arbitrarily:

Group 1: 20 patients selected according to level of LAP
  a. Immediately after bypass: 7.0–9.8 cm H_2O
  b. After transfusion: 14.0–16.6 cm H_2O
Group 2: the 30 patients, selected according to level of pulmonary arterial oxygen saturation
  a. Immediately after bypass: 62–67%
  b. After transfusion: 71–78%

Results

Table 1 summarizes the data obtained during the immediate postperfusion period and after transfusion in 20 patients (Group 1). At an average mean LAP of 8.14 ± 0.84 cm H_2O before transfusion, the mean cardiac index was 2.19 ± 0.51 L/min/m^2, mean MLVP 2.69 ± 1.61 gm-m/min/m^2, average systemic resistance 3,795 ± 1,182 dynes sec cm^{-5}, mean arterial pressure 84.9 ± 19.4 mm Hg, and mean pulmonary artery oxygen saturation 65.9 ± 5.01% (range, 57.5 to 75.5). When LAP was increased by transfusion to an average of 15.2 ± 0.69 cm H_2O, the mean cardiac index rose to 2.77 ± 0.67 L/min/m^2, mean MLVP to 4.08 ± 1.24 gm-m/min/m^2, mean arterial pressure to 104.1 ± 14.8 mm Hg, and mean pulmonary artery oxygen saturation to 75.6 ± 5.7% (range, 66.5 to 86), while average systemic resistance was 3,975 ± 1,412 dynes sec cm^{-5}. Thus, increasing LAP from an average of 8.1 to 15.2 cm H_2O in these 20 patients resulted in a significant increase by the paired *t*-test [4] in cardiac index, MLVP/m^2, arterial pressure, and pulmonary artery oxygen saturation ($p < 0.01$ for these determinations). There was no significant change in systemic resistance.

Data from the 30 Group 2 patients are shown in Table 2. When pulmonary artery saturation was at an average of 65.4 ± 1.6%, the mean of the mean LAP determinations was 7.01 ± 2.66 cm H_2O (range, 1.5 to 13.0), mean cardiac index 2.05 ± 0.52 L/min/m^2, MLVP 2.62 ± 0.80 gm-m/min/m^2, and mean arterial pressure 81.2 ± 16.6 mm Hg. When the pulmonary artery saturation was raised to 74.9 ± 1.54%, mean LAP was 14.7

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*American Optical Co, Bedford, MA 01738.

Table 1. Data from 20 Patients before Transfusion and after Increasing Left Atrial Pressure by Transfusion

	Before Transfusion (LAP = 8.14 ± 0.84)			After Transfusion (LAP = 15.2 ± 0.69)		
Weight (kg)	CI (L/min/m^2)	MLVP/m^2 (gm-m/min/m^2)	PAS (O_2 Sat [%])	CI (L/min/m^2)	MLVP/m^2 (gm-m/min/m^2)	PAS (O_2 Sat [%])
8.6	2.9	3.1	67	3.3	4.0	73
12.2	2.2	1.8	70.5	2.5	3.3	81.5
12.8	2.1	2.5	64	2.5	3.5	71
13.4	1.9	2.0	72	2.5	3.6	82.5
13.6	2.0	1.7	63	2.3	2.7	72.5
15.0	1.9	1.6	66.4	2.3	2.3	71.4
16.8	3.4	3.3	70.5	4.1	6.6	85.5
18.1	2.0	2.0	64	2.4	3.7	70.5
19.1	2.2	3.3	75.5	2.4	3.7	80.0
19.2	2.1	2.4	68.5	2.3	3.1	74.0
21.3	2.3	2.3	62.6	3.0	5.0	76.2
22.9	2.4	6.2	68	2.3	4.1	67.4
27.7	2.4	3.5	68.5	2.5	4.5	74.5
33.9	2.8	3.2	64	4.0	5.6	78.6
34.5	1.4	1.3	63	1.9	2.5	76
40.6	1.8	1.8	58	2.5	3.5	72
42.4	1.5	1.7	64.5	3.6	5.6	81.5
47.1	1.8	3.4	58	2.8	4.3	70.5
47.2	2.9	4.4	73	4.0	5.5	86
66.5	1.7	2.3	57.5	2.2	3.4	66.5
Mean	2.19	2.69	65.9	2.77	4.08	75.6
SD	0.51	1.61	5.01	0.67	1.24	5.7

LAP = left atrial pressure; CI = cardiac index; MLVP = mean left ventricular hydraulic output power; PAS = pulmonary artery saturation; O_2 Sat = oxygen saturation; SD = standard deviation.

± 4.5 cm H_2O (range, 6.2 to 24.8), mean cardiac index 2.67 ± 0.47 L/min/m^2, MLVP 3.73 ± 0.95 gm-m/min/m^2, and the mean of the mean LAP determinations was 102.9 ± 16.6 mm Hg. Using the paired t-test, there was a significant improvement ($p < 0.01$) in MLVP in patients whose total interval of myocardial ischemia was less than 10 minutes when the pulmonary artery oxygen saturation was increased from 65 to 75%; the same was true of patients who were exposed to greater than 10 minutes of myocardial ischemia ($p < 0.01$). Average oxygen consumption after perfusion was 98.4 ± 23 ml/min/m^2. The decreased oxygen consumption (below usual resting levels) was associated with pulmonary artery saturations in a relatively normal range.

Comment

Measurement of LAP, cardiac index, hydraulic output power, and systemic vascular resistance after perfusion permit recognition of significant hemodynamic abnormalities. Generally, intraoperative and postoperative hemodynamic monitoring is limited to central venous and arterial pressures, and it is assumed that cardiac output and performance are adequate if these measurements are within "normal" limits. Data from Table 1 indicate that this may not be the case.

Although emphasis has been placed on postoperative monitoring in the intensive care unit [8, 9], we believe that intraoperative assessment of cardiac performance after bypass yields information that can improve patient care and also provides prognostic information concerning myocardial performance in the critical postoperative period. Intraoperative measurement of LAP, cardiac index, systemic vascular resistance, hydraulic output power, and pulmonary artery saturation provides direct information

Table 2. Data from the 30 Patients before Transfusion and after Increasing Oxygen Saturation by Transfusion

		Before Transfusion (PAS = 65.4 ± 1.6)		After Transfusion (PAS = 74.9 ± 1.54)		
Weight (kg)	IT (min)	CI (L/min/m^2)	LAP (cm H_2O)	CI (L/min/m^2)	LAP (cm H_2O)	Qo_2 (cc/min/m^2)
8.6	15	2.86	5.0	3.32	15.0	137
12.2	26	2.00	3.7	2.36	6.2	109
12.8	0	2.1	7.4	2.6	19.2	122
13.4	23	1.35	6.7	2.3	18.0	78
13.6	21.5	2.00	9.0	2.3	17.8	110
14.5	3	2.10	5.8	2.41	12.5	73
15.0	35.5	1.87	8.3	2.68	22.5	110
16.1	20.5	1.8	3.5	2.54	10.7	83
16.8	0	3.3	7.1	3.7	8.8	126
17.0	16	2.7	5.2	3.4	12.0	109
18.1	0	2.0	7.5	2.54	21.0	84
19.1	1	1.43	4.5	1.56	18.3	59
19.1	0	2.21	7.2	2.34	21.0	95
19.1	0.5	1.54	4.3	2.18	9.3	80
19.2	14.5	1.79	6.6	2.37	12.2	74
19.5	22.0	1.56	6.2	2.34	11.3	76
19.8	0	2.2	6.1	2.6	11.5	108
20.7	17.5	2.86	10.7	2.68	17.1	108
21.3	0	2.26	7.0	2.72	13.0	97
22.9	26.5	2.18	5.0	2.82	12.2	111
23.8	0	1.2	1.5	2.1	12.2	73
27.7	21.5	1.50	11.5	2.5	15.0	65
33.9	27	2.8	7.5	3.5	11.3	125
34.5	24	1.57	9.8	2.7	13.7	81
40.6	29.5	2.23	13.0	2.61	17.0	93
40.9	40.0	1.74	10.2	2.57	17.5	95
42.4	46.0	1.48	7.5	2.96	12.5	104
47.1	19.0	2.83	12.6	3.65	18.8	165
47.7	20.0	2.00	6.0	2.83	10.0	98
66.5	22.5	1.97	9.7	2.90	24.8	104
Mean	16.4	2.05	7.01	2.67	14.7	98.4
SD	13.2	0.52	2.66	0.47	4.5	23.1

IT = myocardial ischemia time; Qo_2 = oxygen consumption; other abbreviations same as for Table 1.

regarding the immediate adequacy of cardiac performance. Parr and colleagues [9] have stressed the importance of maintaining a cardiac index of greater than 2.0 L/min/m^2 and a mixed venous blood oxygen tension above 30 mm Hg. They observed that sudden cardiac death is more often predictable when using both determinations. These authors also emphasized that monitoring arterial pressure alone is insufficient for evaluating the adequacy of cardiac output. Kirklin [6] has suggested a cardiac index over 2.4 L/min/m^2 as generally adequate; when the cardiac index was less than 1.8 L/min/m^2 he noted a significant fatality rate.

Intraoperative measurement of cardiac index and hydraulic output power after correction of tetralogy of Fallot provides a means of identifying those patients in whom a persisting right ventricular outflow gradient is not well tolerated. This information may be obtained while the patient is still in the operating room and facilities for reinstitution of perfusion are at hand. This procedure was applied to a patient who had tetralogy of Fallot with extreme right ventricular outflow obstruction (Fig 1). Intraoperative measurements after initial correction had indicated inadequate left ventricular hydraulic output power as LAP was increased. There was significant improvement after the right ventricular outflow repair was revised. It is important to be cautious about interpreting changes in MLVP with respect to myocardial function, because heart rate and systemic vascular resistance were not controlled; our data were obtained in a clinical setting where it was impractical to regulate all factors influencing cardiac performance such as heart rate and systemic vascular resistance.

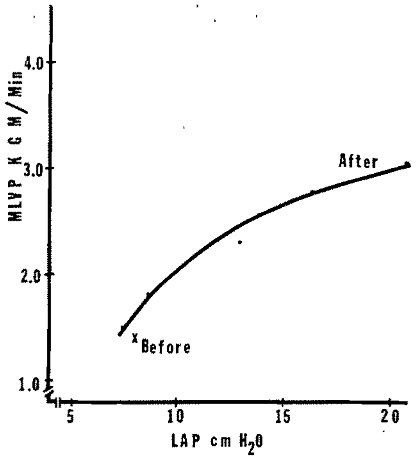
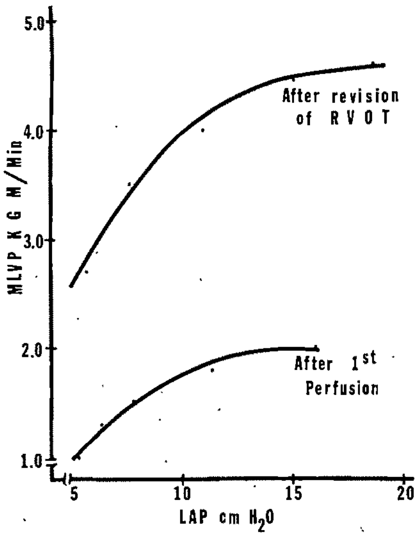


Fig 2. Mean left ventricular hydraulic output power (MLVP) *versus left atrial pressure* (LAP) *before and after cardiopulmonary bypass in a representative patient.*

The principles also apply to the prebypass circulatory status (Fig 2): a severe reduction in hydraulic output power would not be recognized if reliance were placed solely on arterial pressure monitoring. This has been recognized only since we began making measurements of cardiac output before bypass. This information has resulted in greater emphasis on the need for blood transfusion—sometimes in excess of measured loss—during preparation of the patient for bypass. In other instances anesthetic agents have caused myocardial depression and further decreased the already low output.

Fig 1. Mean left ventricular hydraulic output power (MLVP) *versus left atrial pressure* (LAP) *obtained after an initial attempt to relieve right ventricular outflow tract* (RVOT) *obstruction in a patient with tetralogy of Fallot. Following revision of the RVOT obstruction, increased MLVP is noted at each LAP increment. (Heart rate and systemic resistance were not controlled.)*



We have previously emphasized the discrepancy between central venous pressure and LAP [2]. As blood is transfused, these pressures rarely increase by the same increments. Therefore we believe separate measurement of LAP is necessary to determine the filling pressure of the left ventricle. The most practical and reliable indication of this pressure is the LAP measurement, which provides an accurate guide for blood replacement. Crexells and co-workers [5] have previously emphasized the importance of continuously maintaining an optimum filling pressure in patients with acute myocardial impairment in order to increase cardiac output and stroke work. They also noted that administration of potent diuretics may lower left ventricular filling pressure to normal levels and critically reduce cardiac output.

We noted that whereas 1 patient required an LAP of 3.5 cm H_2O to provide a pulmonary artery oxygen saturation of 65.5%, another patient required an LAP of 13.0 cm H_2O for a saturation of 66.5%. Similarly, 1 patient required an LAP of 6.2 cm H_2O to produce a pulmonary artery saturation of 77% while another required 24.8 cm H_2O for a saturation of 74.5%.

This study suggests that pulmonary artery oxygen saturation may be used as a guide to the adequacy of cardiac output. If the pulmonary artery saturation is over 65%, cardiac output should be satisfactory. All 30 patients included in Table 2 survived and were discharged from the hospital. This suggests that patients who have the capacity to increase their pulmonary artery saturation from 65 to 75% have adequate myocardial function.

Reduced oxygen consumption during sedation or anesthesia has been well documented [1, 11–13]. Wilson and associates [13] observed increased oxygen consumption associated with spontaneous efforts at breathing following cardiac operations. Although an impaired left ventricle may maintain an adequate cardiac output under conditions of sedation and respiratory support, it may not produce sufficient blood flow to meet metabolic needs as oxygen consumption increases during recovery from anesthesia. If left ventricular filling pressure is kept high, the resultant rise in cardiac output is more likely to be adequate. It is speculated that in some instances, after a successful intraoperative course, the increase in oxygen consumption may account for the patient's progressive deterioration in the intensive care unit. This circumstance occurs when myocardial function is so impaired that cardiac output cannot be raised to a level necessary to meet the greater metabolic needs of the body.

It is evident from this study and that of Parr, Blackstone, and Kirklin [9] that arterial pressure or LAP alone is inadequate as a guide to cardiac performance. It is also clear that selecting any single indicator of cardiac performance and using it as the sole guide to patient management is unwise. Our intraoperative data confirm those of Osborn and colleagues [8], who concluded from postoperative measurements that the mixed venous saturation is of more clinical value than cardiac output in patient management. Therefore we suggest that a composite of measurements is desirable for precise patient care in the operating room, especially if myocardial function has been compromised. It is also suggested that an LAP level be determined that is associated with a pulmonary arterial oxygen saturation greater than 65%. This approach is usually not necessary in patients with uncomplicated deformities—eg, atrial septal defect—but is recommended for the more complex anomalies, especially if long intervals of myocardial ischemia are used during perfusion. It should be recognized that in some instances recovery from myocardial ischemia or impairment occurs rapidly after an operation and that maintaining a high LAP is unnecessary.

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The Influence of IPPB, CPAP, and IPPB with CPAP during Cardiopulmonary Bypass on Postbypass and Postoperative Pulmonary Function

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ABSTRACT **Pulmonary compliance and shunt ($\dot{Q}_S/\dot{Q}_T$) were employed to determine the optimal method for maintaining the lungs during cardiopulmonary bypass in 100 calves. The calves were divided into four groups with respect to pulmonary maintenance during bypass: nonventilation with the lungs collapsed (Group 1); nonventilation with the lungs exposed to 5 cm H_2O of continuous positive airway pressure (CPAP) (Group 2); intermittent positive-pressure breathing (IPPB) without CPAP (Group 3); and IPPB with 5 cm H_2O of CPAP (Group 4). All groups had similar compliance preoperatively and sustained significant decreases 30 minutes after bypass. Lung compliance returned to preoperative levels two hours postoperatively in Groups 1 and 2 but was still reduced in Groups 3 and 4. The $\dot{Q}_S/\dot{Q}_T$ was markedly higher postoperatively in Groups 3 and 4 than in Groups 1 and 2.**

These data demonstrate that ventilation during bypass reduces early postoperative lung compliance and increases $\dot{Q}_S/\dot{Q}_T$, and they suggest that static pulmonary inflation during bypass offers no advantages over allowing the lungs to remain collapsed.

Maintaining the lungs during cardiopulmonary bypass in such a way as to ensure optimal pulmonary function following bypass is a controversial subject. The reasons for this are that carefully controlled studies are difficult to perform in patients undergoing open-heart operations, and few experimental animal data are available. In this study we evaluated a number of methods for maintaining the lungs during bypass in calves in terms of their effects on postbypass and postoperative pulmonary compliance and pulmonary shunting.

Methods

The experimental subjects were 100 healthy, 92 to 100 kg Holstein bull calves, 8 to 12 weeks old, undergoing implantation of a pneumatically driven artificial heart. Each animal was anesthetized with 350 to 500 mg of sodium methohexital (Brevital Sodium), intubated, and ventilated with 100% oxygen. Before and after cardiopulmonary bypass, ventilation was accomplished utilizing a volume-limited respirator in a humidified, nonrebreathing circuit. A pressure manometer was attached to the endotracheal tube adapter and a Wright spirometer to the exhalation valve. The respirator was adjusted to produce a tidal volume of 15 ml per kilogram of body weight at a rate of 10 to 15 breaths per minute in order to keep arterial carbon dioxide tension (Pa_{CO_2}), as measured every 15 minutes from a femoral artery catheter, between 30 and 35 torr.

Anesthesia was maintained with intermittent 1 to 2 mg/kg doses of ketamine and 0.5 mg/kg doses of succinylcholine every 20 to 30 minutes intravenously. The calves were placed in the supine position and a sternal-splitting thoracotomy was performed. After cardiopulmonary catheters were inserted in the right carotid artery and inferior and superior venae cavae, cardiopulmonary bypass was initiated

The extracorporeal system (Bentley oxygenator, Sarns roller pump) was primed with 2.5 liters of lactated Ringer's solution and 0.5 liter of low-molecular-weight dextran. Anticoagulation was maintained with 5 mg/kg of heparin. Mixed venous blood samples were obtained at the venous inflow to the oxygenator every 15 minutes and were analyzed on a

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Radiometer acid-base analyzer for Po_2, Pco_2, and pH. Bypass flows were maintained between 50 and 70 ml/kg/min to keep mixed venous Po_2 between 38 and 42 torr. Whole cow blood was administered as needed to maintain bypass flow above 50 ml/kg/min. Esophageal temperature was monitored with a Yellow Springs temperature probe. All animals were cooled to 28°C during bypass and rewarmed to 39°C (normal for a calf) at its conclusion.

Methods of maintaining the lungs during bypass included: nonventilation with the lungs collapsed (Group 1); nonventilation with the lungs exposed to a continuous positive airway pressure (CPAP) of 5 cm H_2O from an anesthesia circle system delivering an oxygen flow of 1 liter/min (Group 2); ventilation or intermittent positive-pressure breathing (IPPB) with 100% oxygen at a rate of 6 breaths/min and tidal volume of 10 ml/kg without CPAP (Group 3); and IPPB with 5 cm H_2O of CPAP (Group 4). Calves were randomly assigned one of the four study groups prior to anesthesia induction; each group consisted of 25 animals.

A silicone rubber or polyurethane elliptical type of artificial heart was used in these investigations; it has been previously described [20–22]. The heart is composed of four chambers (two artificial atria and two artificial ventricles), contains four Björk-Shiley pyrolytic carbon disc valves, and weighs approximately 300 gm. Each ventricle consists of a rigid outer casing and a pliable inner blood-containing chamber, between which compressed air is introduced for compression and ejection of blood. Two air-drive lines bring compressed air from a control module (standing next to the calf) through the chest wall to the artificial ventricles within the calf's chest. In the implantation procedure the natural heart is excised, leaving the right lateral portion of the right atrium with its superior and inferior vena caval orifices and the bases of both atria. Silastic artificial left and right atria are sutured to the remnants of the natural atria. The artificial heart is then attached to the natural pulmonary artery and aorta by standard woven Dacron arterial grafts and to the artificial atria by a quick-connect cinch mechanism. The pulmonary artery and aortic grafts and the artificial right and left atria contain taps to which pieces of high-pressure intravenous tubing are connected and brought outside the chest for blood sampling and pressure measurement.

Following implantation of the artificial heart, bypass was terminated and the artificial heart output was adjusted, by heart rate and air driving pressure manipulations [20–22], to maintain mixed venous (pulmonary artery) oxygen tension ($P\bar{v}_{O_2}$) within normal limits (38–42 torr) [22]. Following this, tubes for drainage of both pleural cavities were implanted, the thoracotomy incision was closed, and the animal was placed in the prone position.

Effective pulmonary compliance was measured immediately following anesthesia induction and intubation (study period A) by dividing tidal volume by peak inspiratory pressure measured at the endotracheal tube. Compliance was also measured prior to opening the chest cavity (study period B), before bypass (study period C), 30 minutes after bypass and just before chest closure (study period D), and two hours postoperatively (study period E). The pulmonary shunt ($\dot{Q}_S/\dot{Q}_T$) was measured during study periods D and E. The $\dot{Q}_S/\dot{Q}_T$ was determined by obtaining pulmonary artery and aortic blood samples; measuring Pco_2, Po_2, and oxygen content in these samples with a Radiometer blood gas machine, an American Optical Company oximeter, and standard equations; and utilizing the modified shunt equation:

$$\dot{Q}_S/\dot{Q}_T = \frac{(PA_{O_2} - Pa_{O_2}) \times 0.0031}{(Ca_{O_2} - C\bar{v}_{O_2}) + (PA_{O_2} - Pa_{O_2}) \times 0.0031}$$

in which $PA_{O_2} = P_B - P_{H_2O} - Pa_{CO_2}$

where PA_{O_2} = partial pressure of oxygen in alveolar air, Pa_{O_2} = partial pressure of oxygen in arterial blood, P_{H_2O} = partial pressure of water in pulmonary alveoli (47 torr), Pa_{CO_2} = partial pressure of carbon dioxide in arterial blood, P_B = barometric pressure, Ca_{O_2} = content of oxygen (ml) in 100 ml of arterial blood, and $C\bar{v}_{O_2}$ = content of oxygen (ml) in 100 ml of mixed venous blood.

Results

Mean weight, duration of bypass, blood replacement during bypass, and blood loss for two hours postoperatively were similar in all four

Table 1. Preoperative, Intraoperative, and Postoperative Data in 100 Calves Having the Lungs Maintained by Various Methods during Operation[a]

Group[b]	Weight (kg)	Bypass Time (min)	Bypass Blood Replacement (ml)	Two Hour Postoperative Blood Replacement (ml)
1	95 ± 2	123 ± 9	2,687 ± 235	427 ± 62
2	94 ± 1	119 ± 8	2,549 ± 198	399 ± 76
3	94 ± 2	122 ± 11	2,713 ± 211	418 ± 51
4	94 ± 1	121 ± 9	2,532 ± 241	391 ± 60

[a] All values are mean ± standard deviation.

[b] Group 1 = nonventilation with the lungs collapsed; Group 2 = nonventilation with the lungs exposed to 5 cm H_2O of CPAP; Group 3 = IPPB without CPAP; Group 4 = IPPB with 5 cm H_2O of CPAP.

groups (Table 1). One or both pleurae were entered prior to bypass in all animals. When compared with control values (study period A), compliance was unchanged before the chest cavity was opened (study period B); significantly increased ($p < 0.025$) just before bypass (study period C); and significantly decreased ($p < 0.025$) 30 minutes following bypass (study period D) in all animals (Table 2). Compliance was not greatly different from control values two hours postoperatively (study period E) in Groups 1 and 2 but was still significantly depressed in Groups 3 and 4 at this time ($p < 0.05$). There was no marked difference in compliance between the groups during study periods A, B, and C, but Groups 3 and 4 had significantly lower compliance than Groups 1 and 2 ($p < 0.05$) 30 minutes following bypass and two hours postoperatively (study periods D and E).

The shunt fraction could not be measured prior to study periods D and E. All groups had markedly higher $\dot{Q}_S/\dot{Q}_T$ values during study period D than in E ($p < 0.05$) (Table 3). $\dot{Q}_S/\dot{Q}_T$ was significantly lower in Group 1 animals than in the other groups during study period D ($p < 0.05$). Groups 1 and 2 had similar $\dot{Q}_S/\dot{Q}_T$ levels during study period E, and both values were substantially lower than those for Groups 3 and 4 during this period.

Comment

In spite of adequate venting of the left side of the heart, improved pump oxygenators, and better preoperative preparation and intraoperative management, respiratory distress after open-heart procedures is still fairly common [8, 15] Some of these disturbances are related to the primary pathological process [3, 19] and others

Table 2. Effective Pulmonary Compliance before, during, and after Cardiopulmonary Bypass (Mean ± SD)

		Compliance (ml/cm H_2O) by Study Period				
Group	Pulmonary Management	A (following intubation)	B (prior to thoracotomy)	C (prior to bypass)	D (30 min postbypass)	E (2 hr postop)
1	No ventilation, no CPAP	92 ± 9	89 ± 11	105 ± 12[a]	76 ± 9[a]	88
2	No ventilation, CPAP	90 ± 7	91 ± 10	106 ± 13[a]	74 ± 9[a]	84
3	IPPB, no CPAP	91 ± 8	88 ± 12	106 ± 9[a]	60 ± 10[a,b]	79[b,c]
4	IPPB + CPAP	90 ± 8	89 ± 10	108 ± 14[a]	61 ± 8[a,b]	77 ± 13[b,c]

[a] $p < 0.025$, Student's paired t-test, when compared to values during study periods A and B.

[b] $p < 0.05$, Student's unpaired t-test, when compared to values in Groups 1 or 2 during this period.

[c] $p < 0.05$, Student's paired t-test, when compared to values during study periods A and B.

Table 3. Pulmonary Shunt after Bypass and Postoperatively (Mean ± SD)

	Shunt (%) by Study Period	
Group	D (30 min postbypass)	E (2 hr postop)
1	23 ± 6^{a}	$16 \pm 4^{b,c}$
2	31 ± 8	$19 \pm 3^{b,c}$
3	36 ± 9	27 ± 6^{c}
4	38 ± 9	27 ± 5^{c}

[a] $p < 0.05$, Student's unpaired t-test, when compared to values in Groups 2, 3, and 4 during this period.

[b] $p < 0.05$, Student's unpaired t-test, when compared to values in Groups 3 and 4 during this period.

[c] $p < 0.05$, Student's paired t-test, when compared to values during period D.

to invasion of the pleural cavities [8]. However, another source of postoperative respiratory dysfunction may be improper management of the lungs during bypass.

Although there have been numerous investigations concerned with the influence of cardiopulmonary bypass on postbypass respiratory dynamics [14, 16, 18, 23, 24], few have carefully examined and compared different methods of managing the lungs during extracorporeal circulation [4, 8, 10]. Furthermore, what little information is available on the subject is conflicting. Thus, whereas Kottmeier and co-workers [10] found significant peribronchial hemorrhage and alveolar collapse in dog lungs allowed to remain deflated during bypass—which did not occur when the lungs were ventilated at 10 to 15 breaths/min—Cartwright and associates [4] demonstrated that ventilation (IPPB) was more detrimental to canine pulmonary compliance during bypass than allowing the lungs to remain collapsed. Cartwright's group also showed that keeping the lungs statically inflated during bypass offered no advantages, with respect to pulmonary compliance, over allowing them to remain passively deflated. In contrast, Ghia and Andersen [8] found that human lungs develop a high alveolar-arterial oxygen tension gradient, increased airway resistance, and decreased compliance after cardiopulmonary bypass if allowed to remain statically inflated at 5 cm H_2O pressure during bypass but that this could be completely avoided by inflating the lungs to a pressure of 25 to 30 cm H_2O every 5 minutes.

The reasons for conflicting findings in these studies are not clear but could be related to a host of factors, including different experimental protocols and methods of studying pulmonary function during and after bypass, the modifying influence of a variety of anesthetic agents that could themselves alter pulmonary mechanics, different pump and oxygenator priming fluids and methods of conducting bypass, variable bypass and postbypass cardiovascular dynamics, and different animal species. Our study attempted to avoid these inconsistencies and difficulties while investigating various popular methods for maintaining the lungs during bypass. This was accomplished by employing healthy animals from a single species, utilizing an anesthetic agent without significant pulmonary effects, priming the extracorporeal circuit and maintaining bypass in a standard fashion, and controlling postbypass cardiovascular dynamics with our artificial heart control module so that cardiovascular dynamics and total-body tissue perfusion were optimized. Our findings demonstrate that IPPB during bypass, with or without CPAP, reduces postbypass and early postoperative compliance and increases postoperative shunting when compared with lungs that are not ventilated. While the compliance values of nonventilated lungs return to preoperative levels by two hours postoperatively, compliance in ventilated lungs is still significantly depressed at this time. Our data also suggest that static inflation of the lungs during bypass offers no advantages over allowing them to remain collapsed.

That IPPB may be detrimental to unperfused lungs or lungs perfused solely through bronchial vessels has been suggested by a number of authors [7, 14]. Faridy and co-workers [7] found that ventilation of excised unperfused dog lungs increases the minimal surface tension (γmin) of pulmonary extracts of these lungs in direct proportion to tidal volume and duration of ventilation. They also showed that the effects of IPPB could be completely reversed by terminating ventilation, filling the lungs with air, and maintaining them at a constant volume for several hours. Mandelbaum and Giammona [13] have demonstrated that ventilating dog lungs during bypass produces minimal increases in pulmonary surface tension in two hours but marked elevations in four. Whether IPPB during bypass has any influence on pulmonary surface tension and alveolar collapse after bypass or postoperatively is unknown. Since increased pulmonary shunting and decreased compliance can occur with pulmonary congestion [2, 6], following pulmonary surfactant depletion and surface tension elevation [2, 9], as well as after a host of other types of pulmonary insults [2, 6], it is clear that our data do not delineate the mechanism by which ventilation during bypass produces pulmonary dysfunction following bypass.

Continuous positive airway pressure has become increasingly popular in the treatment of patients with atelectasis secondary to chronic obstructive disease [6], surfactant depletion or inactivation [9], pulmonary congestion [6, 11], or posttraumatic pulmonary insufficiency [11]. Much evidence exists indicating that CPAP reduces pulmonary shunting and increases the matching of pulmonary ventilation to perfusion in these disease states [6, 9, 11]. The physiological mechanism of this effect appears to be an increase in functional residual capacity and concomitant prevention of alveolar closure [1, 5, 25]. CPAP has also been extensively used, and apparently is quite effective, in treating pulmonary dysfunction following open- and closed-heart operations as well as that occurring after noncardiac operations [6]. The efficacy of CPAP as a mode of therapy for the increased pulmonary shunting and atelectasis seen during anesthesia and operation is less well established, and its use intraoperatively is considerably more controversial [5, 17, 25]. One of the main reasons for this is that CPAP in anesthetized or hypovolemic patients frequently results in marked reductions in cardiac output [5], which may further worsen ventilation/perfusion matching rather than improving it. Although use of CPAP without IPPB is a common method of maintaining the lungs during bypass [12], no evidence is available that its utilization prevents atelectasis, reduces pulmonary shunting, or improves compliance either during or after bypass when compared with allowing the lungs to remain deflated and unventilated. Indeed, Cartwright and co-workers [4] have shown that compliance during bypass is similar whether the lungs are allowed to remain deflated or are maintained statically inflated. Our data in this study demonstrate that postbypass and postoperative shunting and compliance are also uninfluenced by deflation of the lung during bypass. Our findings suggest, therefore, that nonventilation with either deflated or statically inflated lungs appears at this time to be the optimal method of maintaining the lungs during cardiopulmonary bypass.

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The Effects of Sterilization and Storage Treatments on the Stress-Strain Behavior of Aortic Valve Leaflets

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ABSTRACT **An investigation was made of the feasibility of using tensile tests to detect alterations in the molecular structure of aortic valve tissue brought about by sterilizing or storage treatments. Stress-strain tests were carried out on fresh valve leaflets from pigs and repeated with the same specimens after specified sterilization or storage treatments. It was found that the stress at a given strain was increased by treatment with ethylene oxide, buffered formalin, and tissue culture solution and decreased by treatment with antibiotics. The least change was with tissue culture solution and antibiotics.**

It has been suggested that the best method of allograft sterilization should involve minimal structural alteration to the collagen and elastic components of the tissue. Thus, treatment with tissue culture solution and antibiotics seems appropriate.

Clinical studies indicate that the methods of sterilization and storage of cadaver valves influence their long-term behavior as allografts for the replacement of damaged or incompetent heart valves [1, 6]. Sterilization and storage treatments affect the molecular structure of valve leaflets and therefore their subsequent durability as surgical grafts. Changes in molecular structure, eg, the cross-linking of collagen molecules and ground substance, could also influence the response of the leaflet tissue to stretching. Specifically, the stress (force/cross-sectional area) to produce a given strain (extension/original length) should be sensitive to molecular structure. Thus it appeared that tensile testing, which is the standard engineering tool for determining the stress-strain behavior of materials, might prove a valuable means for quantitating the structural changes brought about by sterilization and storage treatments.

Experimental Methods

Not enough valves were available from postmortem examinations in humans, so the work was done on valves taken from pigs, for they were readily available and microscopically their structure is not markedly different from that of human aortic valves [7]. Characterization of the stress-strain behavior of fresh leaflets in modified Hanks's solution has been described in another paper [9]; the effect of treatment with buffered formalin, antibiotics, ethylene oxide, and tissue culture solution—all of which have been used clinically—is described now. The composition of these solutions is as follows.

Modified Hanks's solution: NaCl, 32.4 gm; KCl, 1.6 gm; $MgSO_4$, 0.4 gm; $MgCl_2$, 0.4 gm; $Na_2HPO_4 \cdot 12H_2O$, 0.48 gm; KH_2PO_4, 0.24 gm; dextrose, 4 gm; H_2O, 3.9 liters

Buffered formalin: 37–40% formalin, 100 ml; H_2O, 900 ml; sodium phosphate monobasic, 4 gm; sodium phosphate dibasic (anhydrous), 6.5 gm

Antibiotics: penicillin, 50 units; streptomycin, 1 mg; kanamycin, 1 mg; amphotericin B, 25 units; modified Hanks's solution, 1 ml

Ethylene oxide: 16 hr in 12% ethylene oxide at atmospheric pressure and 4–5°C (stored before and after in modified Hanks's solution)

Tissue culture solution: Medium 199 (Commonwealth Serum Laboratories, Melbourne), 100 ml; sodium bicarbonate, 0.39 gm; H_2O, 900 ml; pH 7.2–7.4 (fresh)

The method of recovering specimens from the pigs and of tensile testing is given in another

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paper [9]. Briefly, hearts from choppers (3- to 4-year-old pigs, 150 to 225 kg) were placed in plastic bags immediately upon slaughtering. Approximately two hours later the aortic valve leaflets were dissected and stored at 8°C in appropriate solutions until testing; these solutions were either modified Hanks's or one of the sterilizing and storage solutions just described. The storage time did not exceed four days. There was never any sign of gross bacterial contamination. The solutions remained transparent. The leaflets were lightly stretched and specimens 6 × 19 mm were punched from them, taking one specimen from each leaflet in either a circumferential or a radial direction on the leaflet. The specimens were then gripped at each end and mounted in an Instron tensile-testing machine, which applies an axial extension and also measures the force to produce this extension. All testing was done with the specimens immersed.

The first series of tensile tests was performed on fresh valve leaflets that had been stored immediately after collection in one of the solutions at 8°C for four days (except for ethylene oxide, which required only 16 hours). These tests subjected the specimens to repeated cycling ranging from no force to given strains to determine the elastic limit. It was found that all the treated leaflets were completely elastic up to all strains; ie, as with fresh leaflets stored in modified Hanks's solution, the tensile strain up to fracture initiation is completely recoverable [9].

It was established in our other paper that stress-strain curves vary from leaflet to leaflet in a single valve as well as from pig to pig [9]. Therefore, to determine the effect of a sterilizing and storage treatment on the stress-strain curve, the following procedure was followed: (1) A specimen from an unsterilized (fresh) leaflet was cycled in modified Hanks's solution from no load to a given strain to precondition the specimen [9] and establish the stress-strain curve. (2) The same specimen was then immersed, together with the grips, in one of the sterilizing or storage solutions at 8°C for four days (except for ethylene oxide). The relative position of the grips was fixed during treatment by having them clamped to a stainless-steel support that was also immersed in the solution. (3) The specimen was then returned to the Instron machine and was stretched to the given strain level while remaining immersed in the sterilizing or storage solution. The stress-strain curve after the sterilizing or storage treatment was compared with the curve prior to treatment. The procedure was repeated for the remaining sterilizing or storage solutions using a specimen from a different valve. The effect of sterilization and storage treatment on specimens oriented in both radial and circumferential directions was investigated.

A similar procedure was carried out to evaluate the effect of sterilizing and storage treatments on stress relaxation. An untreated specimen was preconditioned by cycling from no force to a given strain [9]. It was then mounted in the Instron machine and stretched to given strains and held at these strains while the decay of stress with time was recorded. The specimen grips and grip supports were then immersed in one of the solutions. After treatment, the stress-relaxation experiments were repeated in the solution. The procedure was also done for other solutions and orientations using different valves.

Results

Stress-Strain Curves

As mentioned, the leaflets were always completely elastic up to the initiation of fracture; ie, the strain returned to zero when the force returned to zero.

Stress-strain curves in both the radial and circumferential direction for specimens before and after treatment are shown in Figures 1 and 2. We had previously estimated the stress in the circumferential direction on a working valve in the closed position caused by a blood pressure of 150 mm Hg; the estimated value was 2.5×10^5 newtons per square meter [9]. As can be seen from Figure 1, the working valve is quite lightly stressed. In fact, the average valve is operating under a (static) safety factor of about 10.

At a given strain, the stress is increased by sterilizing in ethylene oxide or buffered formalin and by storage in tissue culture solution. Antibiotics decrease the stress. The magnitude of the stress changes can be compared if an equivalent strain is defined as the strain measured from a point at which the stress starts to

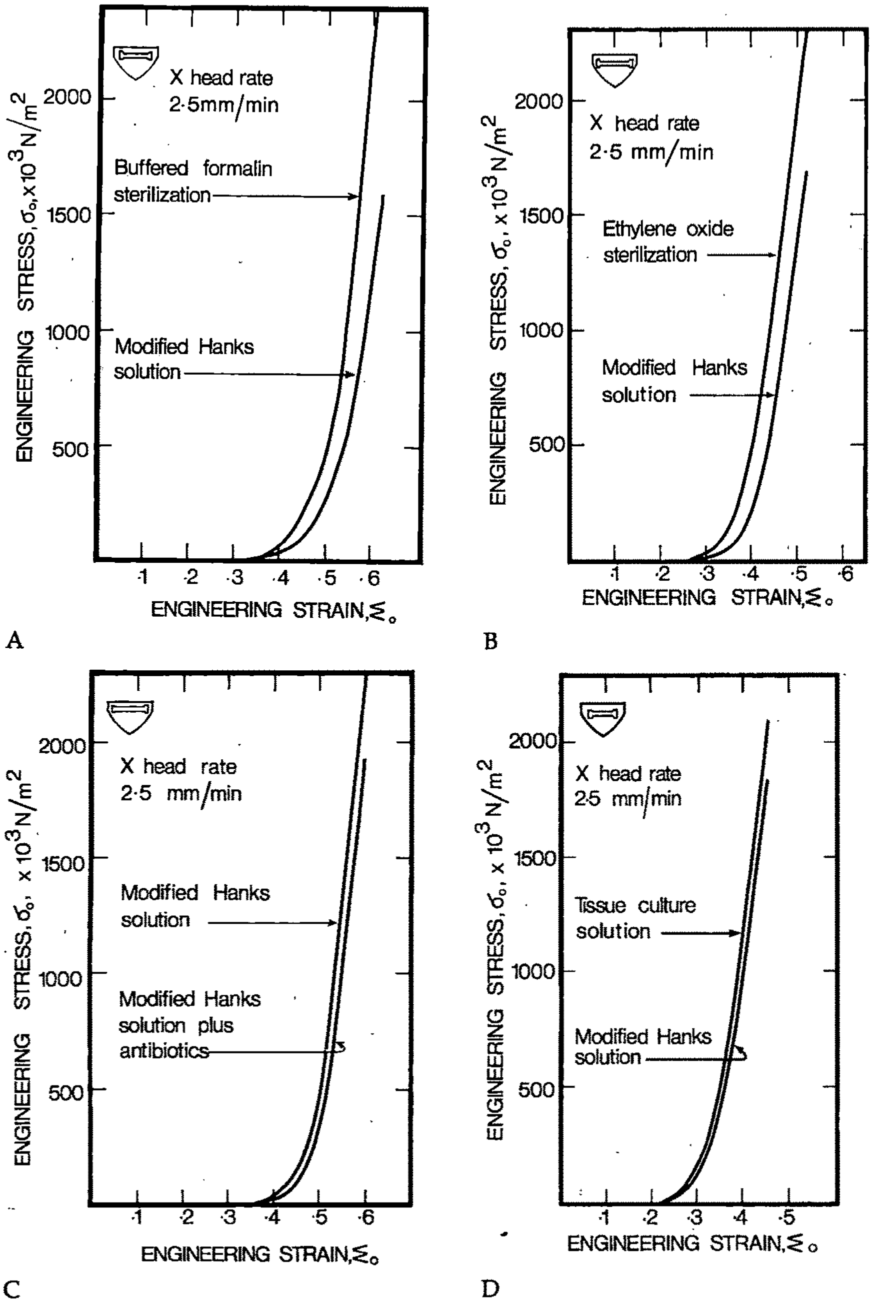

Fig 1. Stress-strain curves for circumferential specimens tested in Hanks's solution and then retested after treatment with various sterilizing and storage solutions: (A) buffered formalin, (B) ethylene oxide, (C) antibiotics, and (D) tissue culture solution.

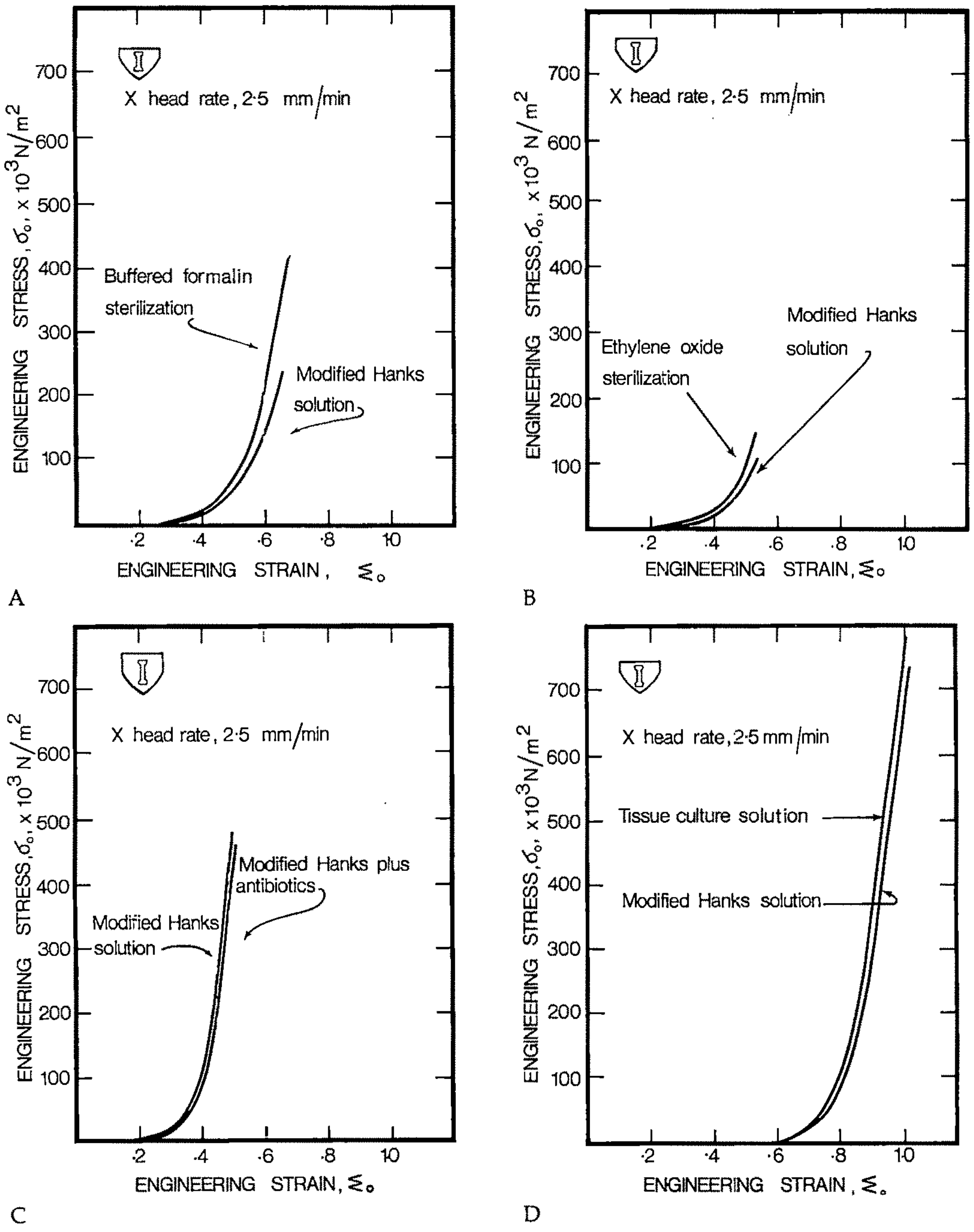

Fig 2. Stress-strain curves for radial specimens tested in Hanks's solution and then retested after treatment with various sterilizing and storage solutions: (A) buffered formalin, (B) ethylene oxide, (C) antibiotics, and (D) tissue culture solution.

Table 1. Percentage Increase in Stress due to Sterilizing and Storage Treatment: Circumferential Direction

	% Increase in Stress			
Equivalent Strain	Hanks's + Antibiotics	Tissue Culture	Buffered Formalin	Ethylene Oxide
0.05		38		
0.10	−49	26		169
0.15	−68	21	61	168
0.20	−47	20	57	102
0.25	−38		80	68
0.30			76	47
0.35			101	

increase appreciably (the beginning of stage II [9]).

Percentage increases in stress, defined as the stress of the treated specimen minus the stress of the untreated specimen, all divided by the stress of the untreated specimen at given equivalent strains, are given in Tables 1 and 2. It can be seen that tissue culture solution affects the leaflets least, while ethylene oxide has the greatest effect, followed by buffered formalin and antibiotics. A graphic representation of the tables is given in Figure 3. To our knowledge these are the only results available on the effect of sterilization and storage treatments on stress-strain curves, although reports have been made of the effect of sterilization on tensile strength [3, 8]. Stress increases due to sterilizing with ethylene oxide or buffered formalin are probably a result of cross-linking of collagen and collagen and ground substance. The stress decrease caused by antibiotics could perhaps be due to strongly basic streptomycin breaking the electrostatic attraction between amino and carboxyl groups along the collagen fibers.*

The stress increase caused by tissue culture solution may be related to the difference in osmolarity of tissue culture and modified Hanks's solution. The former is calculated to have a lower osmotic pressure. Whatever the molecular basis for the effect of treatment, it can be said that the leaflet is altered to various degrees by different treatments. While there is some divergence of

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*Seelye RN: Personal communication, 1974.

Table 2. Percentage Increase in Stress due to Sterilizing and Storage Treatment: Radial Direction

	% Increase in Stress			
Equivalent Strain	Hanks's + Antibiotics	Tissue Culture	Buffered Formalin	Ethylene Oxide
0.10	−52			
0.15	−40			100
0.20	−17			146
0.25	−11		31	96
0.30	− 7	22	41	68
0.35	−10	22	48	56
0.40		27	51	43
0.45		23	57	
0.50		19	69	
0.55		12		
0.60		6		

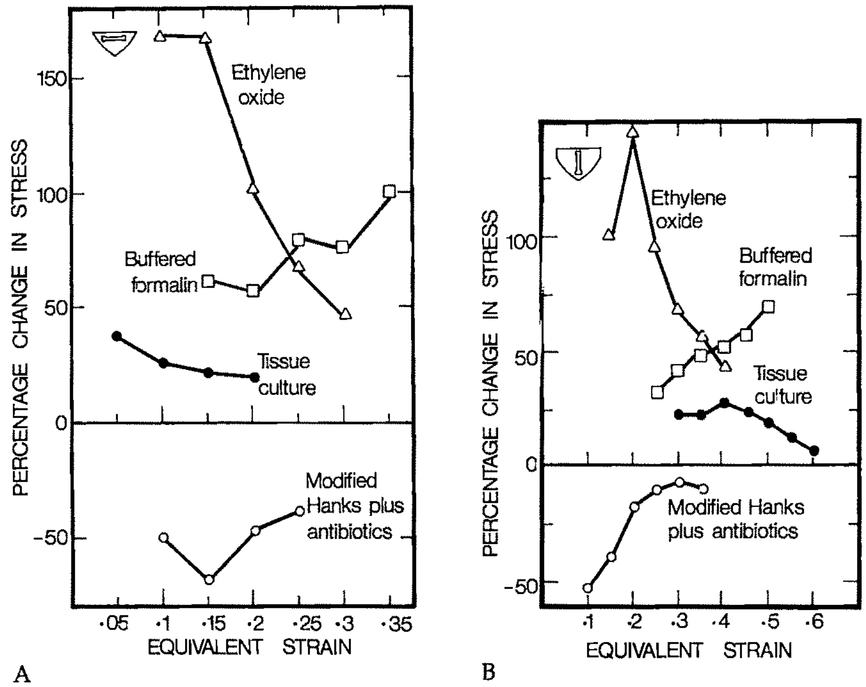

Fig 3. Effect of different sterilizing and storage treatments represented by the percentage change in stress: (A) circumferential specimens, (B) radial specimens.

opinion on the most appropriate methods of sterilization, it appears widely held that the best methods of valve sterilization and storage should involve minimal structural change to the collagen and elastic components [2, 4–6]. Using the stress-strain curves as an indicator of structural change, the best treatment among the methods tested would be either tissue culture solution or antibiotics; such treatments are now favored by Barratt-Boyes and others as a result of clinical experience [6]. Ethylene oxide and buffered formalin would be avoided.

Stress Relaxation

For a given strain, the peak stress (ie, the stress at time zero) on the relaxation curve is increased by treatment with buffered formalin, tissue culture solution, and ethylene oxide. It is decreased by antibiotics. Thus the results of the stress-strain tests are supported by stress-relaxation tests on specimens from different valves. The change in the initial stress is the significant effect of sterilization and storage treatment on relaxation.

Number of Valves Tested

Some consideration of the significance of the results is needed in view of the variability of biological materials. Taking into account both the stress-strain and relaxation tests, valves from 16 animals were tested in all—4 for each sterilization and storage solution. All the tests, both in the radial and in the circumferential direction, gave the same result: ethylene oxide and buffered formalin produced the greatest fractional change in stress level for a given strain and antibiotics and tissue culture the least, with antibiotics producing a lessening in stress. While it may be desirable to do further tests, the present results seem significant. It is also supportive that the findings correlate with clinical experience as to the best treatment for valves.

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Carbon Monoxide Accumulation during Extracorporeal Membrane Oxygenation for Acute Respiratory Failure

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ABSTRACT **A marked increase in the carbon monoxide level in the blood sufficient to interfere with oxygen binding of hemoglobin was observed in a 43-year-old man during the course of extracorporeal membrane oxygenator support for acute respiratory failure from viral pneumonitis. The increased carbon monoxide level in this man was temporally related to the transfusion of large amounts of old bank blood. The etiology of an increased level of carbon monoxide in the blood during extracorporeal circulation is discussed and solutions to this problem are suggested.**

The deleterious effect of a high blood level of carbon monoxide from smoke inhalation is well documented [7]. However, accumulation of a large amount of carbon monoxide in the blood from sources other than atmospheric pollutants — ie, severe red cell destruction and massive transfusion of blood with a high carbon monoxide content — is not well recognized in clinical medicine.

Recently we observed an alarming increase in the carbon monoxide level in the blood, sufficient to interfere with oxygenation of hemoglobin, in a patient undergoing extracorporeal membrane oxygenator support for acute respiratory failure. This report discusses the patient's clinical course and the etiology of increased carbon monoxide concentration in the blood and suggests solutions to this problem.

A 43-year-old man was transferred to Boston University Hospital on May 31, 1974, for possible extracorporeal membrane oxygenation because of refractory hypoxemia secondary to bilateral diffuse pneumonitis, presumably of viral etiology. Prior to being transferred he had received maximal respiratory therapy for three days consisting of continuous positive-pressure ventilation with 100% oxygen concentration in the inspired air ($F_{I_{O_2}}$) and 12 cm H_2O positive end-expiratory pressure (PEEP), vigorous use of diuretics, and fluid restriction.

On admission to the University Hospital he was obtunded with no localizing neurological signs, hypotensive (80/50 mm Hg), febrile (37.8°C), and cyanotic. He weighed approximately 100 kg. A chest roentgenogram showed bilateral diffuse confluent infiltrates. The electrocardiogram was normal. Despite 12 cm H_2O of PEEP ventilation with 100% $F_{I_{O_2}}$, the arterial P_{O_2} was only 37 mm Hg; P_{CO_2} was 57.4 mm Hg. Extracorporeal membrane oxygenation was instituted utilizing a venoarterial circuit (right common femoral vein to left axillary artery) with two 3 m^2 units of Landé-Edwards membrane oxygenator. Blood gases were frequently monitored in the right radial and main pulmonary artery as well as across the oxygenator circuit. Carbon monoxide levels in the venous and arterial outlets of the oxygenator were measured at frequent intervals with a cooximeter.* He was supported with the extracorporeal membrane oxygenator for seven days, and from the third day onward we were able to maintain the arterial P_{O_2} at or above 50 mm Hg with 60% $F_{I_{O_2}}$ and 10 cm H_2O of PEEP at a bypass flow rate of 4.5 to 5 liters per minute. The oxygen delivery by the membrane oxygenator was in the range of 180 to 300 ml per minute.

During the seven days of support, no major bleeding was seen. The calculated intrapulmo-

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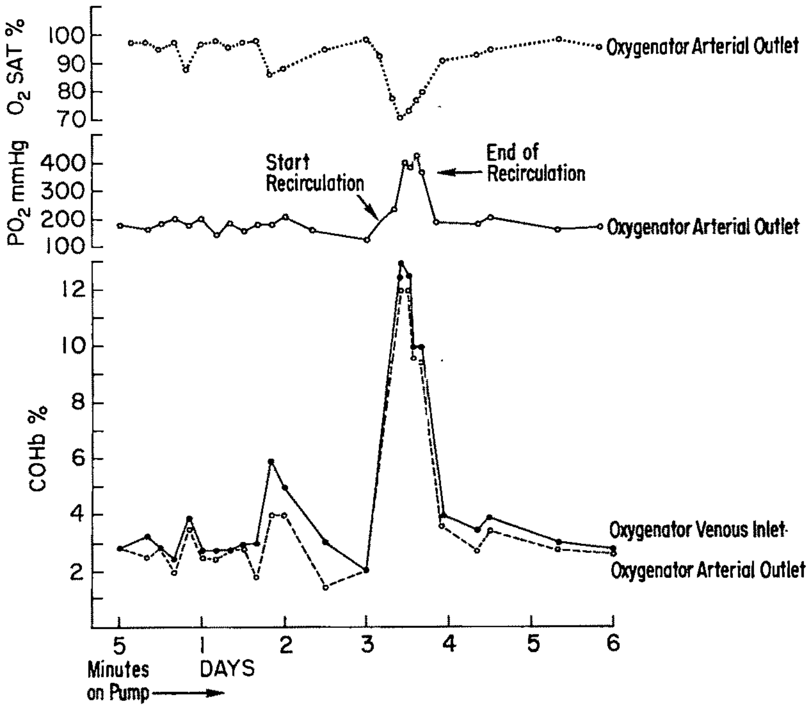
nary shunt fraction decreased from an initial value of 57.7% to a low of 29.1% on the sixth day. Slight improvement in lung compliance was observed, but the dead space–tidal volume ratio (V_D/V_T) did not change appreciably. Peak inspiratory pressure was constantly high (55–58 cm H_2O).

On the fourth day of perfusion a rapidly progressive drop in oxygen saturation at the oxygenator outlet was noted. This was consistently so despite the high Po_2 measured at the oxygenator outlet with a hemoglobin content of 14.5 gm per 100 ml. Hence, 60 to 70% of the blood coming through the oxygenator outlet was recirculated through the membrane oxygenator. Although this maneuver increased the Po_2 at the arterial outlet to a very high level, the oxygen saturation was still low, suggesting impaired oxygen binding by the hemoglobin. Concomitant with this drop in oxygen saturation, the carbon monoxide level in the venous blood gradually rose to an unphysiologically high level of 13% (Figure). Prior to this phenomenon, the patient had received 8 units of old stored blood over a period of four hours. No other patient in the same intensive care unit, with a common source of oxygen supply, demonstrated this disproportion between arterial oxygen saturation and levels of arterial Po_2, thus eliminating inspired air as a possible source of carbon monoxide. Potassium phosphate, 10 mEq, was given intravenously in an attempt to cause a rightward shift in the oxyhemoglobin dissociation curve, thus lessening the deleterious effect of carboxyhemoglobin. In addition, F_{IO_2} was increased to 100% to improve the alveolar oxygen tension and tidal volume was turned up to augment alveolar ventilation, with the hope that by mass action, oxygen would replace the carbon monoxide in the hemoglobin molecule. We set out to watch the trend over the next six to seven hours and were prepared to transfuse red blood cells enriched with 2,3-diphosphoglycerate (2, 3-DPG) to produce a further shift of the oxyhemoglobin dissociation curve to the right.

During this observation period, however, the oxygen saturation at the oxygenator outlet improved concomitant with the decline in carbon monoxide level in the venous blood. The patient

Changes in carbon monoxide level in the blood during extracorporeal membrane oxygenator support in a 43-year-old man in acute respiratory failure. Note the marked increase in the carbon monoxide level on the fourth day, with concomitant drop in oxygen saturation at the oxygenator arterial outlet, despite a marked increase in Po_2 at the arterial outlet effected by recirculating the blood through the oxygenator.



eventually died of gram-negative septicemia two days after he was weaned from membrane oxygenator support. Retrospective analysis of blood gas data revealed modest drops in oxygenator arterial saturation on the first two days of membrane lung support in spite of the adequate oxygenator arterial Po_2. The carbon monoxide level in the blood on these two occasions was 4.0 and 6.8%, respectively. Interestingly enough, transfusions of multiple units of bank blood had been given to the patient several hours prior to the observed reduction in oxygen saturation.

Comment

Carbon monoxide in the blood may be of exogenous or endogenous origin. Exogenous sources include cigarette smoke, automobile exhaust fumes, and byproducts of a wide variety of industrial processes. Recent information indicates that blood from donors who are chronic cigarette smokers has a higher carbon monoxide level than that from nonsmokers [12, 14]. Endogenous carbon monoxide is a byproduct of hemoglobin catabolism. It is ironic that man pollutes his own air simply through renewing his red blood cells and heme-containing enzymes (catalase, peroxidose, myoglobin, and so on). A normal, healthy adult produces about 10 ml per day of carbon monoxide from such heme sources, which raises blood carboxyhemoglobin (COHb) levels to about 0.4%. The threshold limit value for occupational exposure is 50 ppm of carbon monoxide in eight hours, which could produce as much as 8 to 10% COHb, while cigarette smokers who smoke and inhale 10 to 20 cigarettes per day have a COHb level of about 4.5 to 5%.

The bulk of the body store of carbon monoxide is reversibly bound to the red cell hemoglobin. Although there is evidence that a small amount of carbon monoxide is oxidized within the body, virtually all of it is excreted intact in the expired air within approximately three hours [11, 15]. Transfusion of a single unit of blood with an increased level of carbon monoxide may not be serious because the carbon monoxide is diluted in the recipient's blood volume; thus the usual level of carbon monoxide found in the blood from smoking donors may not be a toxic hazard to all patients receiving transfusions. It is potentially dangerous in patients receiving multiple transfusions, however, since no major dilution of transfused blood with the recipient's blood volume occurs, or in subjects who are extremely sensitive to even low levels of COHb: patients undergoing coronary bypass operations [9], patients with coronary artery disease [2] or acute respiratory failure, and infants with erythroblastosis fetalis undergoing exchange transfusion [8].

In patients receiving membrane oxygenator support, several potential mechanisms for increasing the level of carbon monoxide may be present. During blood pumping lasting many days, both obvious outright and sublethal damage to red cells occurs. It has been well established that sublethally damaged red cells have a very short life span [4]. Hence, the catabolism of hemoglobin in large quantities over a short period can result in excessive accumulation of carbon monoxide. Furthermore, clinical experience with extracorporeal membrane oxygenator support has indicated the need for large volumes of blood to be transfused, especially in the first few days of support. If the blood used in such circumstances has a high carbon monoxide level — ie, blood from smoking donors — it could seriously affect the affinity of oxygen for the recipient's hemoglobin.

The rate of carbon monoxide exchange in the lungs during acute respiratory failure is unknown at the present time, although the fast clearance of COHb in our patient's blood would indicate that carbon monoxide exchange capability remains intact. Investigation of carbon monoxide transfer across the membrane lung is lacking. It is probably of small magnitude, as suggested by the narrow venoarterial COHb difference found in our patient and preliminary studies by others* (see the Figure).

Carbon monoxide in the blood reduces the oxygen-carrying capacity of red blood cells because its affinity for hemoglobin is more than 200 times that of oxygen. Carboxyhemoglobin causes a leftward shift of the oxyhemoglobin dissociation curve; hence, tissue oxygenation suffers. The organophosphate 2,3-DPG in the red cells effects a rightward shift of the oxygen dissociation curve. Since the 2,3-DPG level in

*Ramirez RA: Personal communications, 1974.

red blood cells decreases in stored blood, the presence of COHb exaggerates the deleterious leftward shift in the oxygen dissociation curve. Erythrocyte 2,3-DPG levels in stored blood may be maintained by the use of citrate-phosphate-dextrose (CPD) anticoagulants, and decrements in 2,3-DPG can even be reversed by adding nucleosides such as inosine and adenosine [3]. We gave potassium phosphate to our patient with success and did not have to transfuse enriched blood with a high 2,3-DPG level.

Recent observations have documented an increased carbon monoxide level in blood from smoking volunteer donors [12]. Davis and Gantner [6] reported a mean COHb saturation of 4.5% in a large group of volunteer donors who were chronic smokers. They have also shown that a smoking volunteer eliminated one-half of his COHb content in 45 minutes by breathing 100% oxygen. Peterson and Stewart [10] demonstrated an average half-life for COHb of 320 minutes in subjects breathing air free from carbon monoxide.

From this rather unique experience, we think the following precautionary measures are warranted in patients undergoing membrane oxygenator support for acute respiratory failure:

1. Both P_{O_2} and oxygen hemoglobin saturation in the arterial blood at the oxygenator outlet should be monitored frequently during the bypass support.
2. The COHb level should be measured frequently in all patients.
3. Preferably, nonhemic blood volume expanders should be used to keep the perfusion flow at adequate levels in the first few days of support.
4. If transfusion is absolutely necessary, CPD blood with high levels of 2,3-DPG should be used.
5. The COHb level of any blood to be transfused during bypass support should be measured; if it is high, the blood should not be used. The blood bank might label smokers' blood with a high COHb level to designate units with a reduced oxygen-carrying capacity.
6. If fresh blood is needed, smoking donors should be asked to abstain from cigarettes for two hours and to breath oxygen and hyperventilate prior to the phlebotomy.
7. Finally, if carbon monoxide accumulation and low oxygen saturation become serious problems during the bypass, total-body asanguineous hypothermic perfusion washout [1] or treatment in a hyperbaric chamber with two atmospheres pressure [13] should be considered.

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Granular Cell Myoblastoma of the Bronchus: Report of 2 Cases and Review of the Literature

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ABSTRACT **Granular cell myoblastoma of the bronchus is rare. Two patients are described, bringing the total reported to 44. Review of the literature shows that cough, chest pain, hemoptysis, and wheezing are frequent presenting symptoms and that distal atelectasis and recurrent or persistent pneumonitis are common roentgenographic findings. Though the histogenesis of this tumor remains controversial, most pathologists now believe that the cells have a neurogenic origin. Adequate open surgical resection is the treatment of choice.**

Granular cell myoblastoma of the bronchus is rare: only 42 cases have been reported in the English literature. Endobronchial granular cell myoblastoma causes symptoms by obstruction and erosion of the bronchus. Cough, chest pain, hemoptysis, and wheezing are common presenting symptoms. Distal atelectasis, persistent or recurrent pneumonitis, and suppuration are frequent findings on chest roentgenogram, necessitating a differential diagnosis from pulmonary neoplasms and infections. Perhaps more important, because of its local invasiveness and often associated atypical hyperplasia of surface epithelium, it simulates a malignant tumor both grossly and histologically. Continuing recognition of this tumor is therefore important, and it is with this in mind that we add 2 more patients, 1 of them a 10-year-old boy.

Patient 1

A 32-year-old black woman was treated in the emergency room and outpatient clinic for recurrent episodes of "bronchial asthma" for four years prior to her admission to Boston City Hospital. On admission she was in acute respiratory distress with a productive cough, temperature of 39.5°C, bronchial wheezes over the right lung field, and tachycardia. Chest roentgenograms showed right lower lobe consolidation with basal atelectasis. The white blood cell count was 18,000 with a marked shift to the left. The hematocrit was 38%. She responded to appropriate antibiotic therapy and was discharged on bronchodilator therapy but one month later was readmitted with a temperature of 40°C, shortness of breath, and a productive cough with blood-streaked sputum.

Physical examination revealed right-sided inspiratory and expiratory wheezes, dullness at the lung base, and moist rales. A chest roentgenogram showed consolidation of the basal segment of the right lower lobe (Fig 1) with collapse of the right middle and right lower lobes. The consolidation was in the same segment that had been involved at the previous admission. A selective bronchogram showed a filling defect at the lower aspect of the intermediate bronchus that completely obstructed flow of contrast material into the lower lobe bronchus (Fig 2). The middle lobe bronchus was impinged upon at its origin, as seen in the oblique view, but in the anteroposterior projection it appeared patent. Sputum cytology failed to demonstrate malignant cells. Fiberoptic bronchoscopy revealed complete occlusion of the right lower lobe and partial obstruction of the right middle lobe bronchus with a friable, lobulated, grayish, endobronchial mass. The biopsy was consistent with granular cell myoblastoma.

Right lower and middle lobectomies were performed. Grossly, the surgical specimen was a 2×2 cm soft, yellowish gray tumor that had been obstructing the right lower lobe and right middle lobe bronchi, producing atelectasis of these lobes. Microscopically the lung parenchyma showed organizing bronchopneumonia, bronchiectasis, and bronchiolectasis with peribronchiolar fibrosis. There was mucosal hyperplasia as well as metaplasia (Fig 3). Granular cell myoblastoma extended into the orifice of the right

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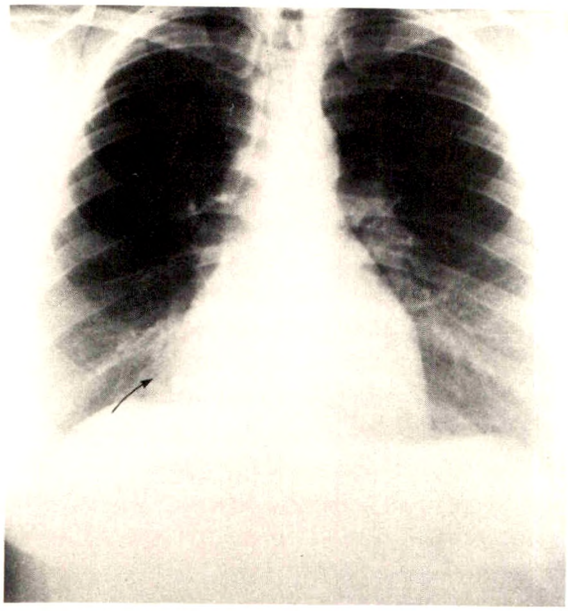

Fig 1. (Patient 1.) Preoperative chest roentgenogram showing atelectasis of the basal segment of the right lower lobe (arrow).

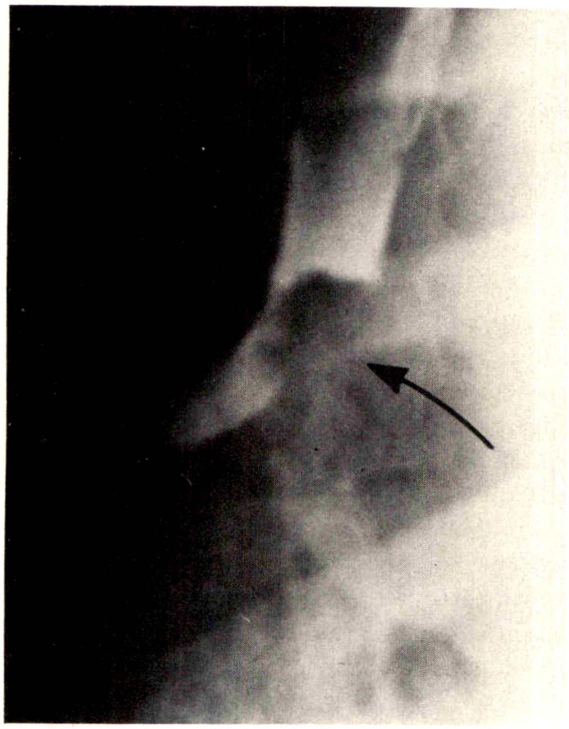

Fig 2. (Patient 1.) Bronchogram showing filling defect caused by tumor obstruction of the right lower lobe bronchus (arrow).

middle lobe and completely obstructed the right lower lobe orifice.

The postoperative course was uneventful, and she was asymptomatic three years after the operation.

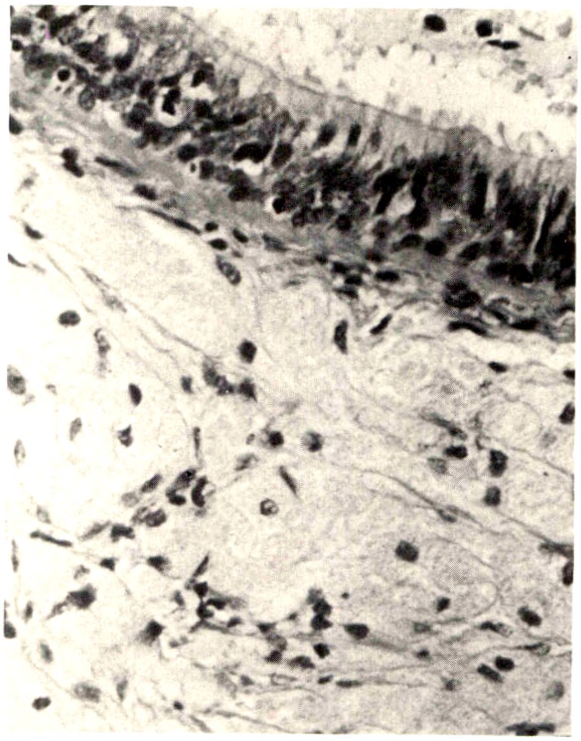

Fig 3. (Patient 1.) Cellular tumor mass that had been occluding the bronchial lumen. (H&E; original magnification ×100.)

Patient 2

The patient was a 10-year-old black boy who had been well until one year prior to his admission, when his father noticed that he tired very easily when playing. Eight months prior to admission the patient had complained of a sharp anterior chest pain associated with shortness of breath. The chest roentgenogram showed a left upper lobe infiltrate. With antibiotic therapy the left upper lobe "pneumonia" improved but the infiltrate persisted. Two weeks prior to admission the patient had a recurrence of left pleuritic anterior chest pain with productive cough. He was afebrile and a chest roentgenogram showed a persistent left upper lobe infiltrate. This was unchanged after two weeks of intensive medical treatment. Skin tests for tuberculosis and fungus were negative, as were sputum smears and cultures for acid-fast bacilli.

Physical examination was unremarkable except for expiratory wheezes heard over the left upper chest. A bronchogram showed extensive saccular bronchiectasis of the left upper lobe with bronchial stenosis. Fiberoptic bronchoscopy revealed total obstruction of the apical segments of the left upper lobe. The lingular segment was open but stenosed. The endobronchial surface had an injected, granular appearance with no obvious endobronchial mass. The white cell count was 7,800 with no leftward shift, and the hematocrit was 40%.

A left upper lobectomy was performed. The gross specimen was a yellowish gray mass that had been partially occluding the left upper lobe bronchial lumen. Microscopically the mass was consistent with granular cell myoblastoma with mucosal squamous metaplasia and hyperplasia. The lung showed bronchiectasis, focal fibrosis, and chronic and acute inflammation.

The postoperative course was uneventful, and the patient was asymptomatic three years after operation.

Comment

Granular cell myoblastoma most often occurs in the tongue; the skin, subcutaneous tissue, and breast are other common sites [23]. Rare locations of this lesion are the larynx [5], trachea [1], bronchus [4, 16], chest wall [13], back, axilla, extremities, and anogenital region. The incidence of the endobronchial variety is about 6% of all granular cell myoblastomas.

Review of the current literature indicates that there have been 42 recorded cases of primary endobronchial granular cell myoblastoma. The 2 patients reported here bring the total number to 44. The age range has been from 8 to 56 years with an average of 37 years. The sex incidence has been equal. Bronchial obstruction and erosion were the basis of the symptoms due to this lesion [9]. Persistent or recurrent cough, chest pain, wheezing, and hemoptysis have been the most common presenting symptoms. Chest roentgenograms usually revealed persistent or recurrent pulmonary infiltrates or atelectasis. Prompt endoscopy and biopsy established the diagnosis in all cases. This lesion tends to originate in the walls of the large bronchi. In 59% the right main bronchus was involved; the left main bronchus was involved in 36% and both bronchi in 5%. Five patients had involvement of the carina. In 2 of these patients the carinal lesion consisted of multiple nodules and in 2 others it was contiguous with the lesion in the main bronchus; in 1 instance there was en bloc involvement of the main bronchus and adjacent lower trachea. Nine of the 44 patients have had multiple lesions, an incidence of about 20%. In 2 patients the tumors occurred in the bronchial tree; the other 7 had involvement of other organs (the tongue in 1, esophagus in 1, and skin in 5).

The gross appearance of the endobronchial lesions ranged from a small, ridgelike thickening of the mucosa to a sessile or pedunculated, polypoid mass that partially or completely obstructed the bronchial lumen. The size of the lesion ranged from several millimeters to 6.5 cm in diameter. The cut surface of the lesion appeared yellowish gray or pink in color. Microscopically, the typical cell of granular cell myoblastoma was a large, polygonal one with finely granular eosinophilic cytoplasm and a small, dark, vesicular nucleus. Such cells were arranged in syncytial masses containing long, fusiform cells with elongated nuclei. More than 50% had squamous metaplasia of the mucosa, and in about 40% the lesion extended through the entire thickness of the bronchial wall into the peribronchial tissue. In only 1 case was there frank pulmonary parenchymal infiltration [15]. The histogenicity of this tumor remains controversial, though most pathologists and oncologists today accept a neurogenic origin [2, 8, 17].

Primary endobronchial granular cell myoblastoma is a benign lesion [6, 11]. Local invasion is not unusual, but no case of distant metastasis has ever been reported. In contrast, 6% of nonendobronchial granular cell myoblastomas metastasize [22]. Metastatic pulmonary granular cell myoblastoma from primary sources outside the thorax does not present clinically as the primary endobronchial granular cell myoblastoma. Spontaneous remission of an endobronchial granular cell myoblastoma has not been reported, although nonendobronchial types are known to regress [3, 12]. Surgical manipulation of the primary lesion may lead to secondary implantation [14]. It is worthwhile to note that bronchoscopic removal of endobronchial myoblastoma has often been followed by recurrence, either by implantation or because of inadequate excision of the tumor [18]. The tumor has invaded the entire bronchial wall in more than one-third of the cases of endobronchial granular cell myoblastoma; in 1 patient there was actual infiltration of the pulmonary parenchyma.

Hence, endoscopic resection of this lesion is not the optimal treatment.

At present there is no evidence to suggest that endobronchial myoblastoma is radiosensitive. Of the 2 patients in the literature who were treated with radium seeds following bronchoscopic excision, 1 had recurrence six years later; there is no long-term follow-up in the second. In contrast, nine- to ten-year follow-up has failed to show recurrence in those patients treated with open resection.

Follow-up has been available for 24 of the patients reported so far. Five were alive and well five to ten years after resection. Eleven patients have been followed for more than three years and are also alive and well. Hemoptysis occurred in 9 patients two years after endoscopic removal, and there have been 2 postoperative deaths.

Adequate open surgical resection is the treatment of choice. This may require a lobectomy [10], with or without sleeve resection of the bronchus [20, 22], and in some instances pneumonectomy [13, 16]. Lesions occurring in the trachea may require resection and reconstruction of the involved segment [1].

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Permanent Extracorporeal Esophagogastric Tube for Esophageal Replacement

Henry J. Heimlich, M.D.

CASE REPORT. A 67-year-old woman with squamous cell carcinoma of the middle third of the esophagus underwent thoracotomy with resection of the esophagus. A proximal cervical esophagostomy was constructed; a gastrostomy tube had been inserted at a previous operation. On the eighth postoperative day, the free end of the gastrostomy tube was inserted into the esophagostomy. The patient was then able to eat a satisfactory diet of all foods that could be chewed into an almost fluid state. It was necessary to apply pressure upon the skin on one side of the tube to prevent leakage. The operation was performed on March 14, 1913, and was reported by Dr. Franz Torek [3]. It was the first successful resection for carcinoma of the thoracic esophagus.

Over the past 60 years, as more satisfactory methods of esophageal replacement were devised, the rubber gastrostomy tube inserted into a cervical esophagostomy became obsolete due to the problem of leakage from the upper end. The need for such tubes can best be avoided by preventive measures. In treating cancer of the esophagus, this is accomplished by proper sequencing of operations. Malignant lesions of the lower third of the esophagus, for example, are resected and reconstructed in one stage using intrathoracic esophagogastrostomy at the level of the aortic arch.

Reconstruction of the esophagus for cancer of the middle and upper third presents few problems when performed as the initial surgical procedure. The lesion is first treated with radiotherapy, then total esophagoplasty is accomplished using a reversed gastric tube, and a few weeks later esophagectomy is performed through a right thoracotomy. If metastases are found at the initial laparotomy for the intended esophagoplasty, an endoesophageal plastic tube with a funnel on its upper end should be inserted to maintain the lumen and enable food to be swallowed. In my original description of this technique, the plastic tube was temporarily sutured to a nasogastric tube in order to draw it downward through a gastrotomy [1]; subsequently, the specially designed Celestin tube was developed. Despite the known complications, insertion of a tube in this manner provides the simplest and most satisfactory palliation.

Surgeons who have resected the esophagus as the primary procedure in treating carcinoma of the middle or upper third frequently find that the patient does not improve sufficiently to tolerate esophagoplasty. The patient is then left with a permanent esophagostomy and gastrostomy, and an external plastic tube bypass might have to be considered. The discomfort of the patient with malignant tracheoesophageal fistula is extreme; however, palliative procedures seldom improve or substantially prolong life. Avoiding any form of operation, including the insertion of extracorporeal tubes, is perhaps the kindest decision in most cases.

Benign lesions should be bypassed in a physiological manner. Esophagoplasty with a reversed gastric tube has been most satisfactory in our hands and can be performed despite previous colon transplant failures, or even after various gastric operations [2]. Colon transplantation can be used if the stomach is not adequate, and should that fail, the small intestine—despite its vascular deficiencies—should be considered for esophagoplasty in preference to an external plastic tube.

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Esophageal Function Tests in the Modern Age of Esophageal Surgery

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The traditional approach to motor abnormalities of the esophagus—represented by the article of Flye and Sealy entitled "Diffuse Spasm of the Esophagus" (Ann Thorac Surg 19:677, 1975)—is subject to diagnostic and therapeutic error that is unnecessary with our available technology.

The clinical differentiation between esophageal spasm, early achalasia, and vigorous achalasia may be exceedingly difficult to make [10]. Classically, the symptoms of achalasia—substernal dysphagia, regurgitation, and weight loss—are distinct from those of esophageal spasm—pain and intermittent obstruction. Patients with vigorous achalasia, however, have clinical features of both achalasia and esophageal spasm: obstruction, regurgitation, and pain. The overlap of symptoms that can occur in these disorders frequently makes their diagnosis based on history alone virtually impossible.

The statement made by Flye and Sealy that "roentgenographic examination of the esophagus is quite distinctive" in diffuse esophageal spasm is not completely valid. The characteristic radiographic "curling" or "corkscrew" esophagus of classic esophageal spasm may be identical to that seen in vigorous achalasia [11]. Alternatively, the barium swallow in esophageal spasm may show mild tapering of the distal esophagus, suggesting early achalasia [8]. Even more perplexing, however, is the completely normal barium swallow examination in some patients with esophageal spasm. Thus, the traditional barium swallow evaluation in patients with motor abnormalities of the esophagus may be misleading or completely nondiagnostic. Further, esophagoscopy contributes little to the evaluation of these patients.

Most of the recent advances in our understanding and diagnosis of the various motor disturbances of the esophagus are the result of data obtained from esophageal function tests, including both manometrics and acid reflux testing with an intraesophageal pH probe. Optimally, these studies should be done routinely both before and after operation in every patient treated for a functional disorder of the esophagus, ie, a condition which impairs swallowing in the absence of intraluminal or extrinsic esophageal obstruction. Only 3 of the patients reported by Flye and Sealy had preoperative esophageal manometric testing. Without question, their patients were carefully evaluated by history, physical examination, roentgenography, and endoscopy. But inclusion of a group of patients with motor abnormalities of the esophagus under the "blanket diagnosis" of esophageal spasm, without manometric confirmation, ignores the most vital diagnostic tool available for these patients.

Esophageal motility studies *alone* are diagnostic of esophageal spasm, achalasia, and vigorous achalasia [2, 3, 10, 11]. Further, acid reflux testing offers the most objective and precise method of evaluating gastroesophageal reflux, being far more sensitive than the barium swallow examination [7, 12]. With acid reflux testing we have demonstrated moderate or severe gastroesophageal reflux in a number of patients with esophageal spasm, epiphrenic diverticula, or both, in whom the barium swallow examination failed to show either a hiatus hernia or reflux. Like Henderson and associates [6], we regard the esophageal spasm in these patients as being secondary to the gastroesophageal reflux, and we differentiate this type of esophageal spasm from the primary form in which there is no other demonstrable etiology. The presence of an associated sliding hiatus hernia in 9 of their 22 patients (41%), however, was thought by Flye and Sealy to be secondary to upward traction on the esophagogastric junction caused by spastic contractions of the longitudinal esophageal musculature. Whether the esophageal spasm is secondary to the hiatus

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hernia and gastroesophageal reflux or the hernia to the spasm, the presence of reflux should be determined preoperatively with acid reflux testing, regardless of the lack of roentgenographic evidence of a hiatus hernia or reflux. An esophagomyotomy performed to relieve esophageal spasm without an associated antireflux procedure to correct the possible etiology is inadequate therapy.

Manometric differentiation between the esophageal motor abnormalities may also alter surgical therapy. As Henderson and associates [6] have recently suggested, primary esophageal spasm may best be treated by extending the esophagomyotomy above the level of the aortic arch. The more routine long esophagomyotomy is adequate for vigorous achalasia and secondary esophageal spasm [4], while distal esophagomyotomy remains the surgical treatment for achalasia [5]. Unless one is prepared to perform the extended long esophagomyotomy advocated by Henderson for primary esophageal spasm in *every* patient with motor disturbances of the esophagus to "cover all possibilities," precise preoperative manometric evaluation is essential.

Not only do preoperative esophageal manometrics and acid reflux testing allow precise diagnosis of motor abnormalities of the esophagus, but they also provide an important baseline against which future postoperative studies can be compared. The incidence of gastroesophageal reflux occurring after esophagomyotomy has not been accurately determined, and it could be with postoperative acid reflux testing. While Ellis and associates [5] limit the distal extent of their myotomy onto the stomach and claim that, because of this, reflux is an uncommon complication, others advocate a deliberate 1 to 2 cm extension of the myotomy onto the stomach to ensure complete division of all circular muscle fibers at the cardia [1]. In the latter situation, conversion of an uncoordinated lower esophageal sphincter mechanism into an incompetent one demands addition of an antireflux operation to prevent the subsequent development of reflux esophagitis.

Routine postoperative acid reflux testing in our laboratory has confirmed the finding of Henderson and associates [6] that a modified Belsey procedure does not adequately prevent gastroesophageal reflux from developing after esophagomyotomy. Combining a Collis gastroplasty with Belsey reconstruction of the esophagogastric junction in patients undergoing esophagomyotomy appears to offer an effective alternative and is currently being evaluated [9].

Only with more universal acceptance and utilization of esophageal function tests in our preoperative and postoperative evaluation of patients with functional disorders of the esophagus will consistent approaches based on firm data be achieved. Thoracic surgeons have accepted sophisticated evaluation and monitoring of our patients with cardiac and pulmonary disorders. Should we settle for less in our patients with esophageal disease?

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Reply

It gives one a sense of pride to realize that one's paper has elicited such a thoughtful and fervent response as that contained in this editorial by Dr. Orringer. A reply arguing against the use of esophageal function tests is difficult to compose. In this day of medicine's infatuation with clinical impedimenta, such a rebuttal puts one in the position of a person spreading scurrilous gossip about Betsy Ross in this, the Bicentennial Year.

Throughout the editorial the distinct clinical entity under discussion is mislabeled. Admittedly, *diffuse spasm of the esophagus* is a poor name; one might say that this is a disorder in search of an eponym. However, it is a real abnormality of unknown etiology, and in no way is it related to or is it to be confused with esophageal spasm associated with acid reflux. Dr. Orringer, of course, realizes this, but he does not clearly say so, implying that reflux may cause the disorder *diffuse spasm of the esophagus.*

The thrust of our paper was that diffuse esophageal spasm can be recognized by history, physical examination, and roentgenographic means. Our success proves our point. We are not opposed to the use of physiological studies, although it is of interest that in Henderson's report—Dr. Orringer's principal authoritative source—the authors failed to make the diagnosis by esophageal function studies in 4 of 21 patients, while retrospectively the condition was evident on roentgenograms in 8 of 11 patients.

Dr. Orringer apparently does not take advantage of the first-rate roentgenologic diagnostic work that must be available to him in Ann Arbor. With a cine recording it is possible to observe esophageal motility repeatedly during swallowing. The signs that Dr. Orringer is familiar with, such as the corkscrew esophagus, are interesting but are not the important ones. The cine film shows that portion of the esophagus involved in diffuse spasm, and if repetitive swallows are observed, one will eventually see the lower sphincter open following a swallow. It is difficult for us to understand how this roentgenographic picture, when correlated with the history, could be confused with spasm of the esophagus caused by reflux.

Although various tests for acid reflux do play a role in the evaluation of esophageal problems, Payne and Olsen [2] have stated that the pH electrode study is of little value to them. To use the results of this test to give a surgeon an excuse for doing a Collis procedure in a patient with diffuse spasm of the esophagus would be regrettable. Even if reflux were present before operation, it would not constitute an indication for this mutilating operation, which permanently destroys the physiological sphincter at the gastroesophageal junction. Without it, our results and those of Ellis [1] have been excellent. Even if reflux had occurred after operation, we would not regret having avoided doing the Collis operation. In fact, the less distortion one produces about the hiatus and gastroesophageal junction, the better; by this we mean a myotomy that just crosses onto the stomach, followed by careful reconstruction of the hiatus. Our only postoperative problem occurred in a patient in whom we did a Belsey repair. She required esophageal dilation after operation.

As for the length of the myotomy in diffuse esophageal spasm, we have elected to extend it to the aortic arch. Our results and those of Ellis prove that this is adequate for relief of symptoms.

This rebuttal is not meant to say that function studies of the esophagus are unimportant, for they have at least shown us the physiological abnormalities in these peculiar esophageal disorders, even though the etiologies still remain obscure. However, as shown by our experience, in overt clinical examples of diffuse spasm of the esophagus they are not essential. In less advanced cases that might not require surgical treatment, these studies may help to identify the patient's problem. If reflux, as determined by pH electrode study, is to be used to promote the Collis operation, then the sum total of its benefit could well be negative.

Will C. Sealy, M.D.
M. Wayne Flye, M.D.

Department of Surgery
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Durham, NC 27710

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CORRESPONDENCE

Superior Vena Cava Obstruction

To the Editor:

In their otherwise very thorough review of the superior vena cava syndrome due to benign causes (Superior Vena Cava Obstruction: A Review of the Literature and Report of 2 Cases due to benign Intrathoracic Tumors, Ann Thorac Surg 20:344, 1975), Gomes and Hufnagel neglected to mention the effects of chronic intravascular foreign bodies. Thrombosis of the superior vena cava, leading to its obstruction, and thrombosis of the deep venous system of the arm have been reported several times in association with permanent transvenous cardiac pacemaker electrodes [1–3, 6], and lesser degrees of thrombosis—on occasion associated with pulmonary embolism [3, 5]—are more common. Within the past year we have encountered symptomatic late deep venous thrombosis (1 month to 2½ years following pacemaker implantation) in 3 of 150 patients with permanent pacemakers being followed regularly in our clinic. In a paper appearing in this issue (p 166) Stoney and his associates report that more than one-third of their patients having elective pacemaker replacment were found by venography to have ipsilateral innominate venous obstruction with well-developed collaterals. Only 21% of their patients with a permanent transvenous electrode in place for 24 months or longer had normal venograms. Similarly, the incidence of thrombosis on transvenous ventriculoatrial shunts for hydrocephalus may approximate 40% [4].

When an intravascular foreign body is present in the superior vena cava in a patient who develops the symptoms and signs of superior vena caval obstruction, the possible etiological role of the foreign body should be considered prior to undertaking an extensive work-up for more serious occult pathology.

G. Frank O. Tyers, M.D.
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Carolyn R. Wine, M.D.

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Insertion of Hancock Xenograft

To the Editor:

It is usually pointless to quibble about minor technical details; however, I believe the hazard posed by a maneuver recommended in a recent article (Stefanik et al, A method for insertion of a stented xenograft valve in the atrioventricular position. Ann Thorac Surg 21:166, 1976) warrants comment.

In the past five years my associates and I have implanted more than 250 Hancock porcine valves in the mitral position and some 25 in the tricuspid position. We have not found it a problem to avoid snaring a suture on the struts of the stent. After all sutures are placed on the annulus and through the sewing ring, they are held straight with gentle tension. It is then quite simple to tilt the valve and to advance it "far edge down" until that edge contacts the rim of the atrioventricular orifice. Usually the far strut will lie inside the ventricle at that stage. The other two struts are clearly exposed and can be inserted into the ventricle under direct vision, easily avoiding entrapment of sutures. Finally, as a last precaution, once the valve is seated and *before any sutures are tied,* the cusps can be gently opened and the two hidden struts examined from inside the valve with a small dental mirror (10 mm diameter). The third strut is clearly visible without the mirror. We have never found a trapped suture but still continue this practice because of the catastrophic consequences that could result if entrapment did occur. In that event, it would be simple to unseat the valve and reposition it.

I strongly oppose the suggested technique of suturing the struts for two obvious reasons: someone is going to injure one or more of the delicate cusps when cutting out the retaining suture, and placing the suture on the fabric covering of the stent risks tearing the fabric or weakening a suture line of the stent cover. Either of these serious injuries would be difficult to detect.

Two of the major characteristics of the Hancock valve are the precision and care with which it is assembled and the delicacy of the natural tissue cusps. Every effort must be made to avoid injury to the cusps or damage to the stent assembly. We carefully clean our gloves; while placing sutures we hold the valve only with a small hemostat carefully placed on the edge of the suture ring; and we keep the tissues moist at all times by frequent bathing with lactated Ringer's solution. We avoid all unnecessary manipulation of the tissue elements of the preparation.

Julio C. Davila, M.D.

Henry Ford Hospital
2799 W Grand Blvd
Detroit, MI 48202

Reply

To the Editor:

Dr. Davila indicates two major points of opposition to the technique that we previously published in *The Annals* to prevent suture entanglement on the struts of the Hancock prosthesis during valve placement. The first is that injury to one or more of the valve cusps might occur when the retaining suture is being cut out. This, of course, is a point of real concern, and one must accomplish the removal of this suture with care. I must emphasize, however, that this is done under direct vision, and injury to the cusps is highly unlikely if one exercises only the usual amount of caution.

The second point of opposition is that injury to the fabric on the stent or weakening of the suture line on the stent might occur during placement of the retaining suture. This possibility was a matter of concern to us. Prior to performing this technique, we thoroughly investigated the matter with Warren Hancock of the Hancock Company, directly inquiring whether or not this would be injurious to the valve. He replied that he was certain it would not be as long as one exercised reasonable care in inserting the suture. It is true that fraying of the fabric from insertion of the suture and its removal could conceivably occur. The Dacron covering, however, generally does not fray; and again, if one exercises reasonable caution in inserting the suture one should not have a problem.

Incidentally, personal communication with Warren Hancock reveals that his company continues to work on a device that will accomplish the same end as our published technique without the necessity of pulling the struts together with a retaining suture.

Finally, I would like to admonish those individuals who use mirrors to visualize the hidden cusps that the insertion and withdrawal of the laryngeal mirror through the valve can also produce cusp injury if one does not exercise the usual reasonable care.

George G. Lindesmith, M.D.

1136 W Sixth St
Los Angeles, CA 90017

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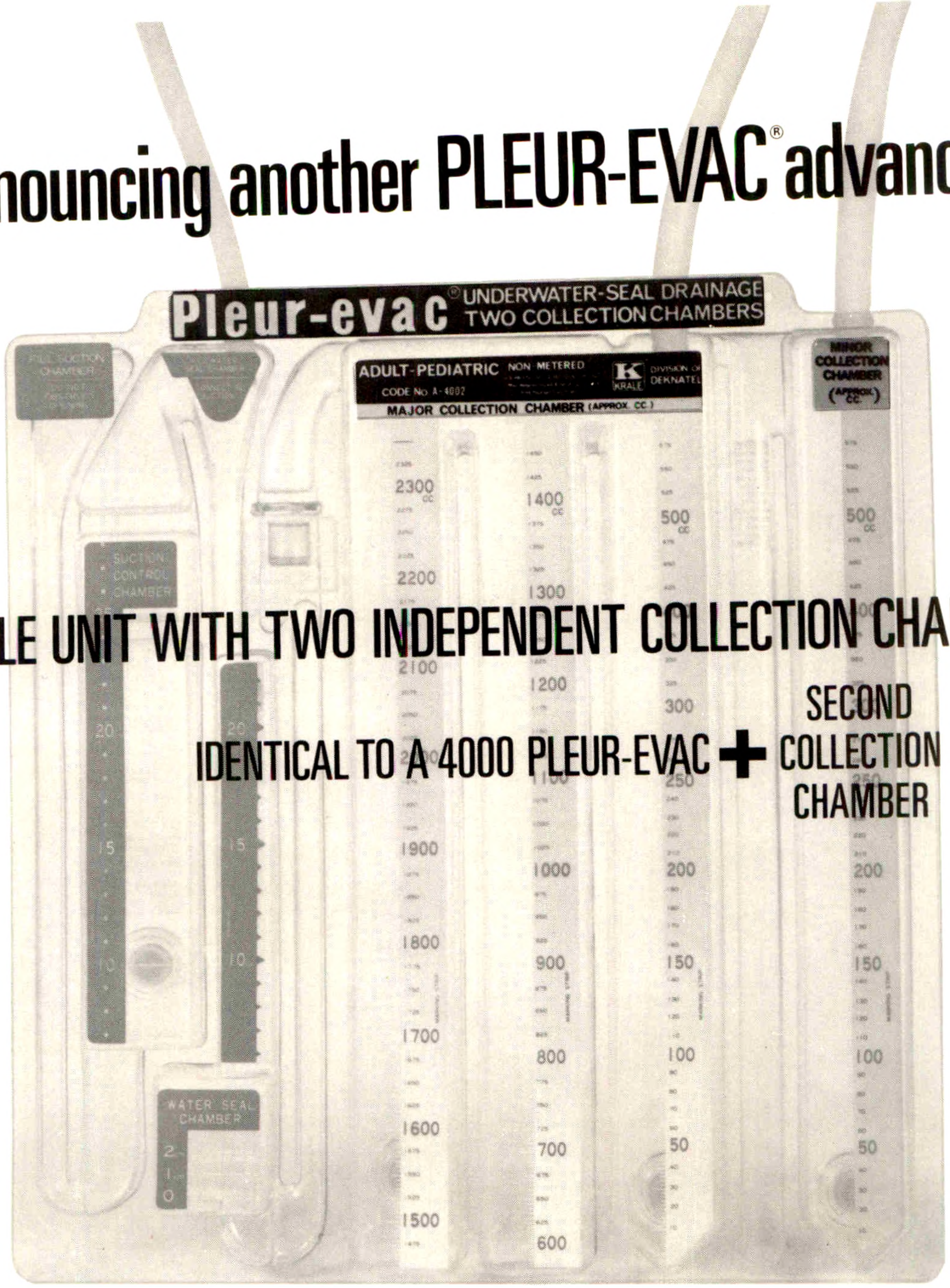

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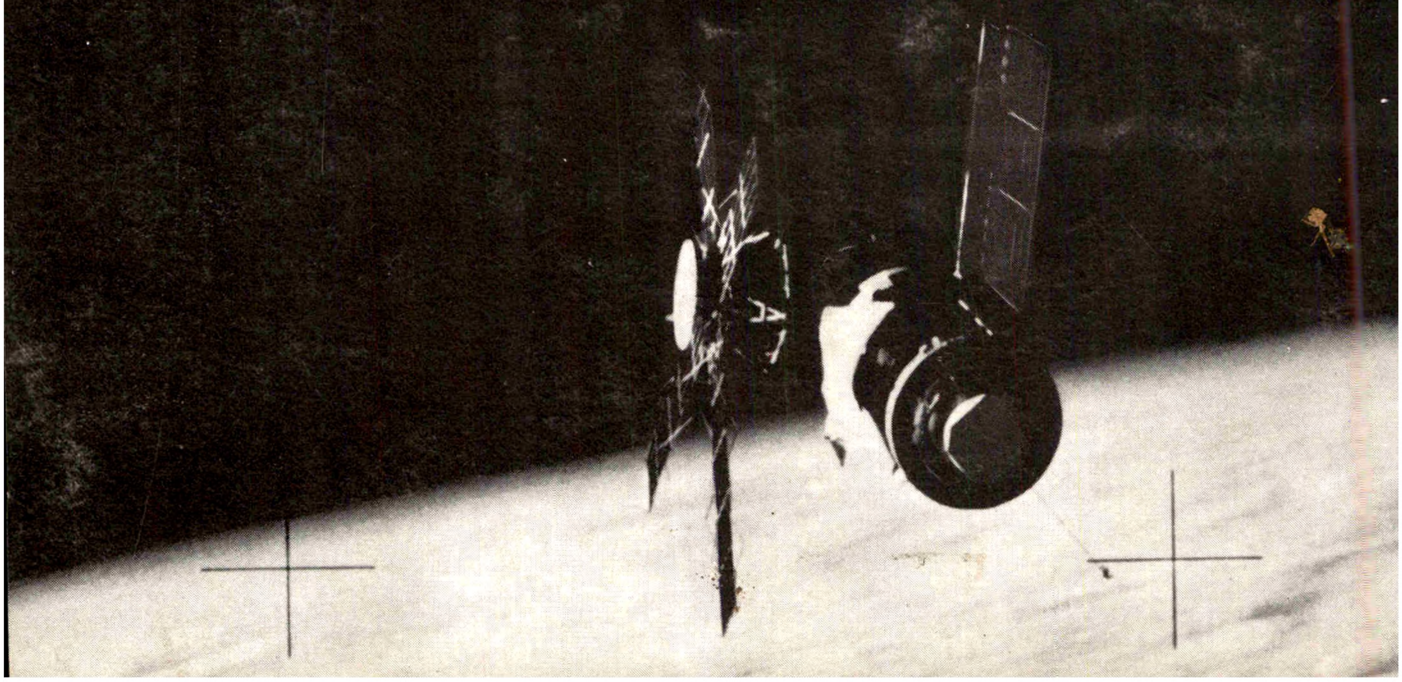

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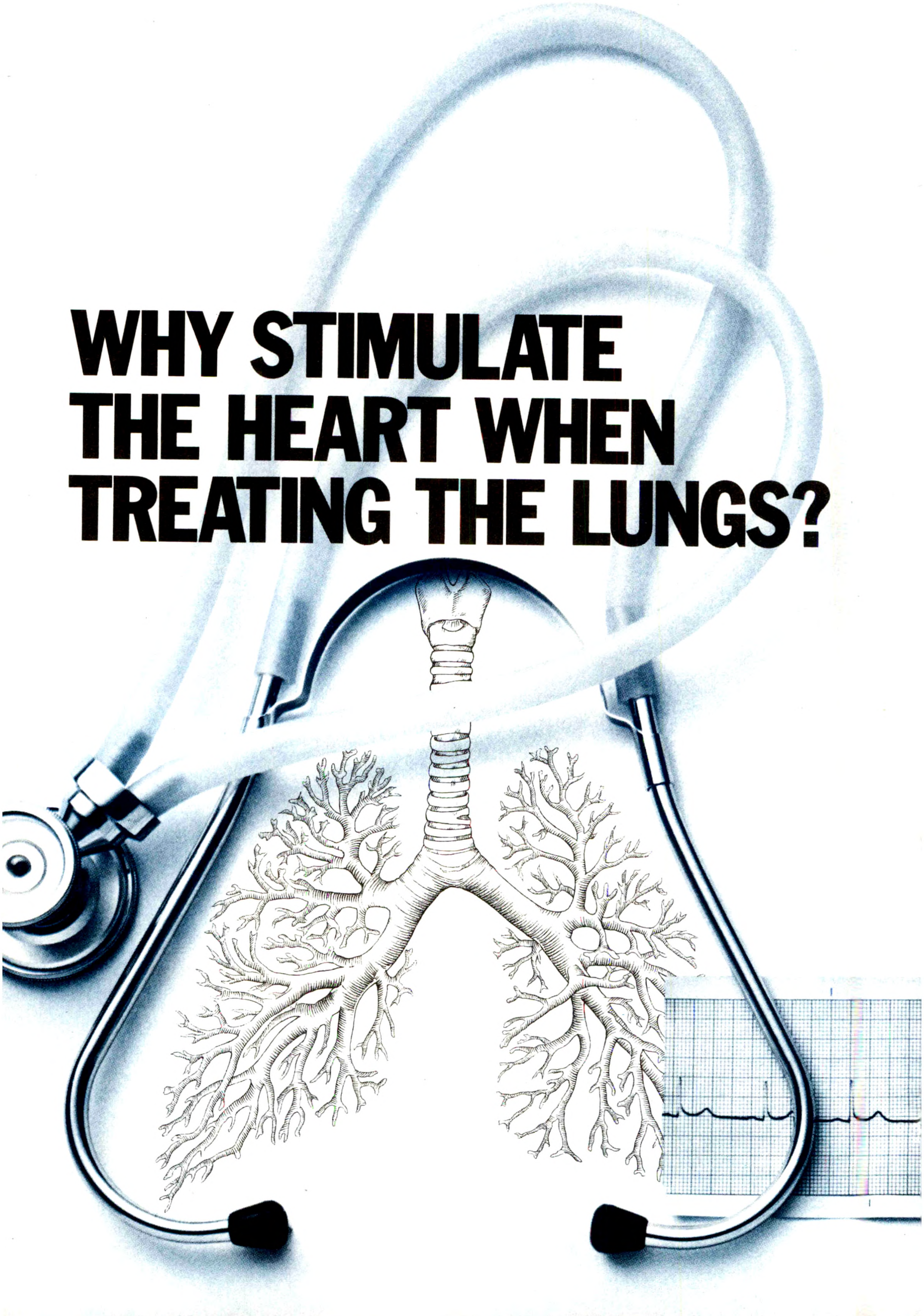
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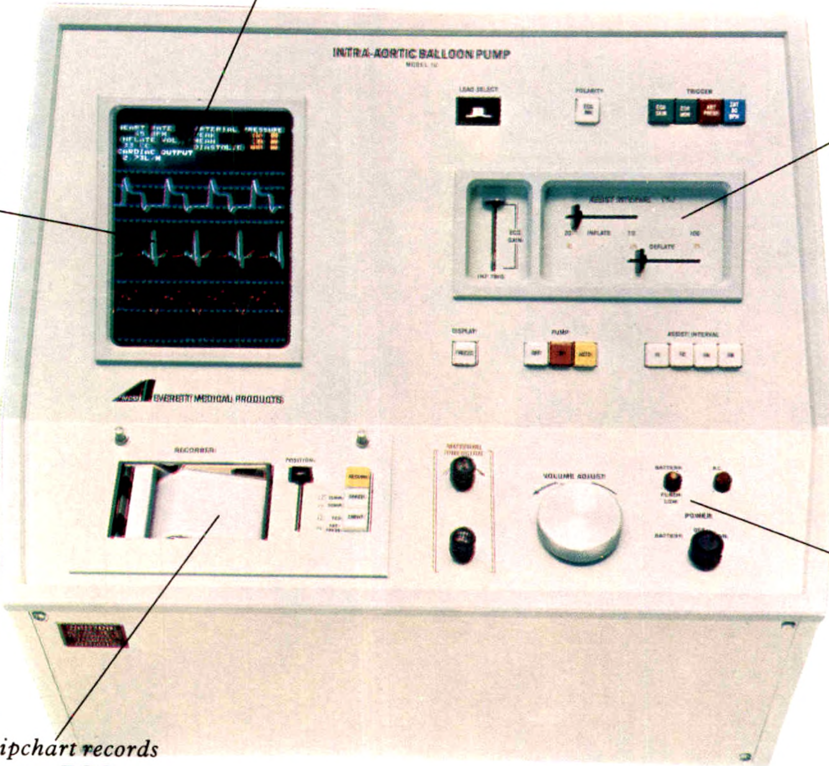

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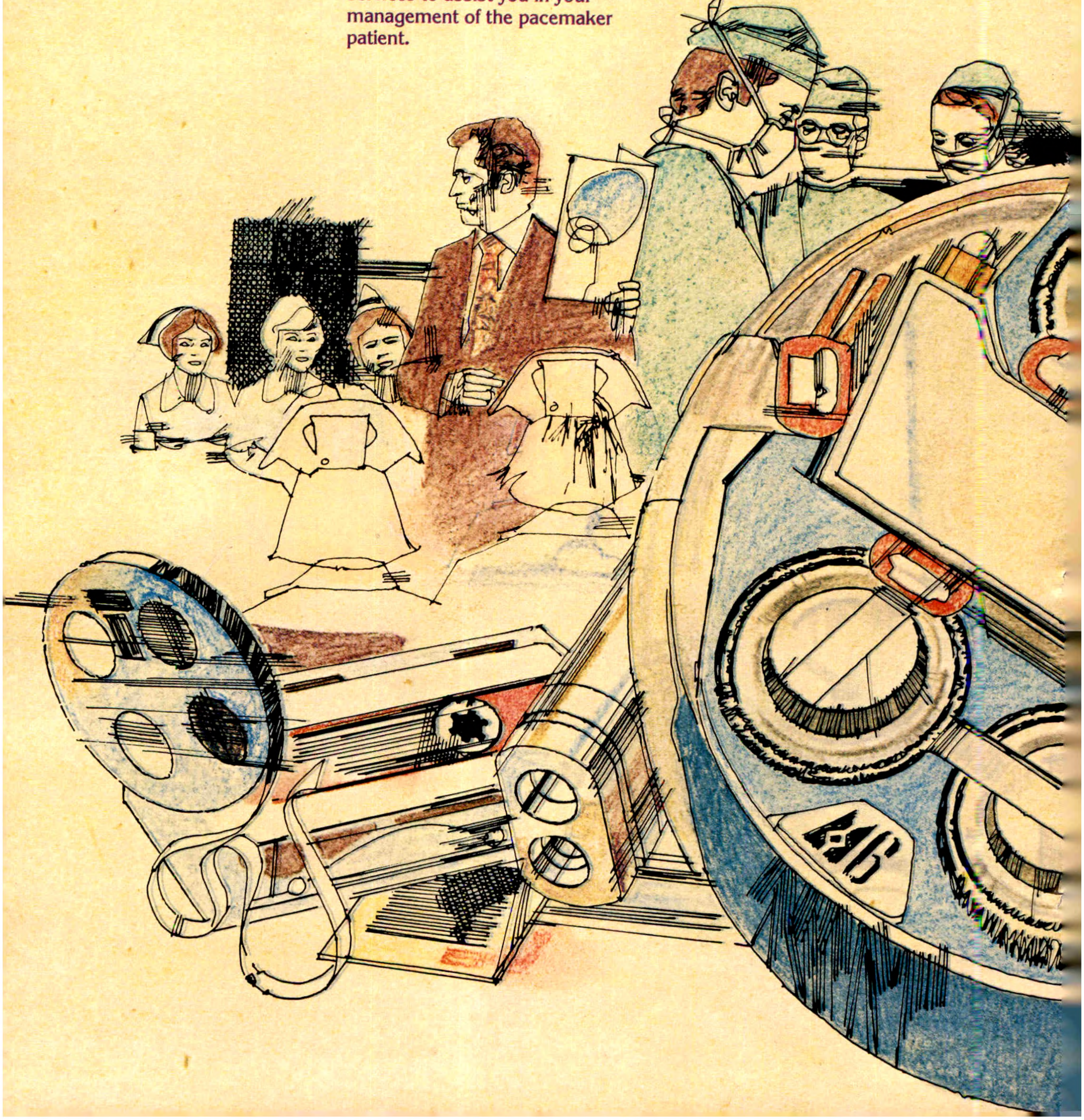

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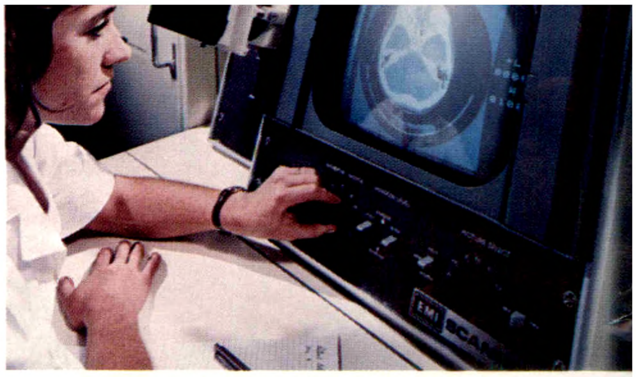

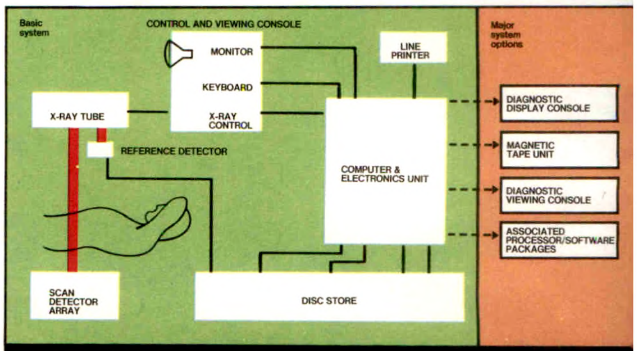

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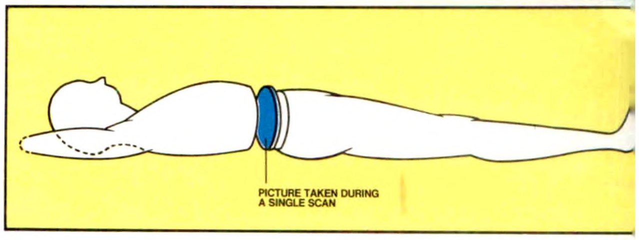
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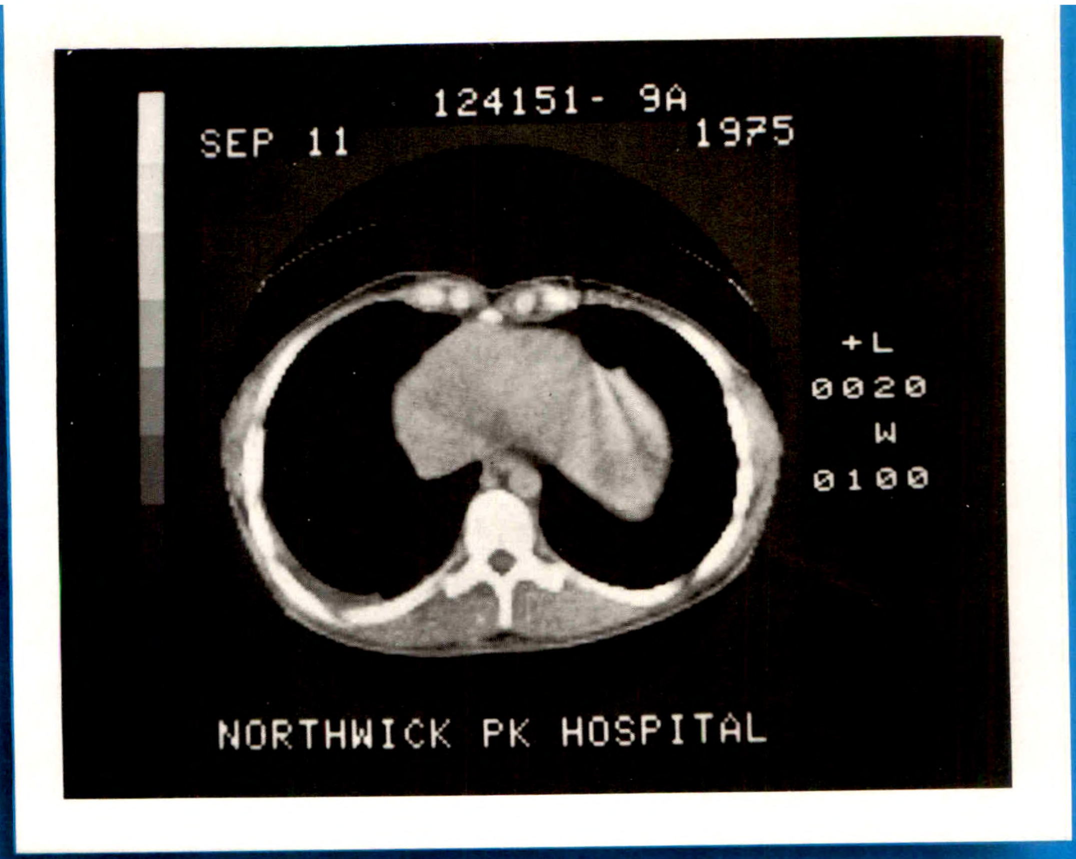

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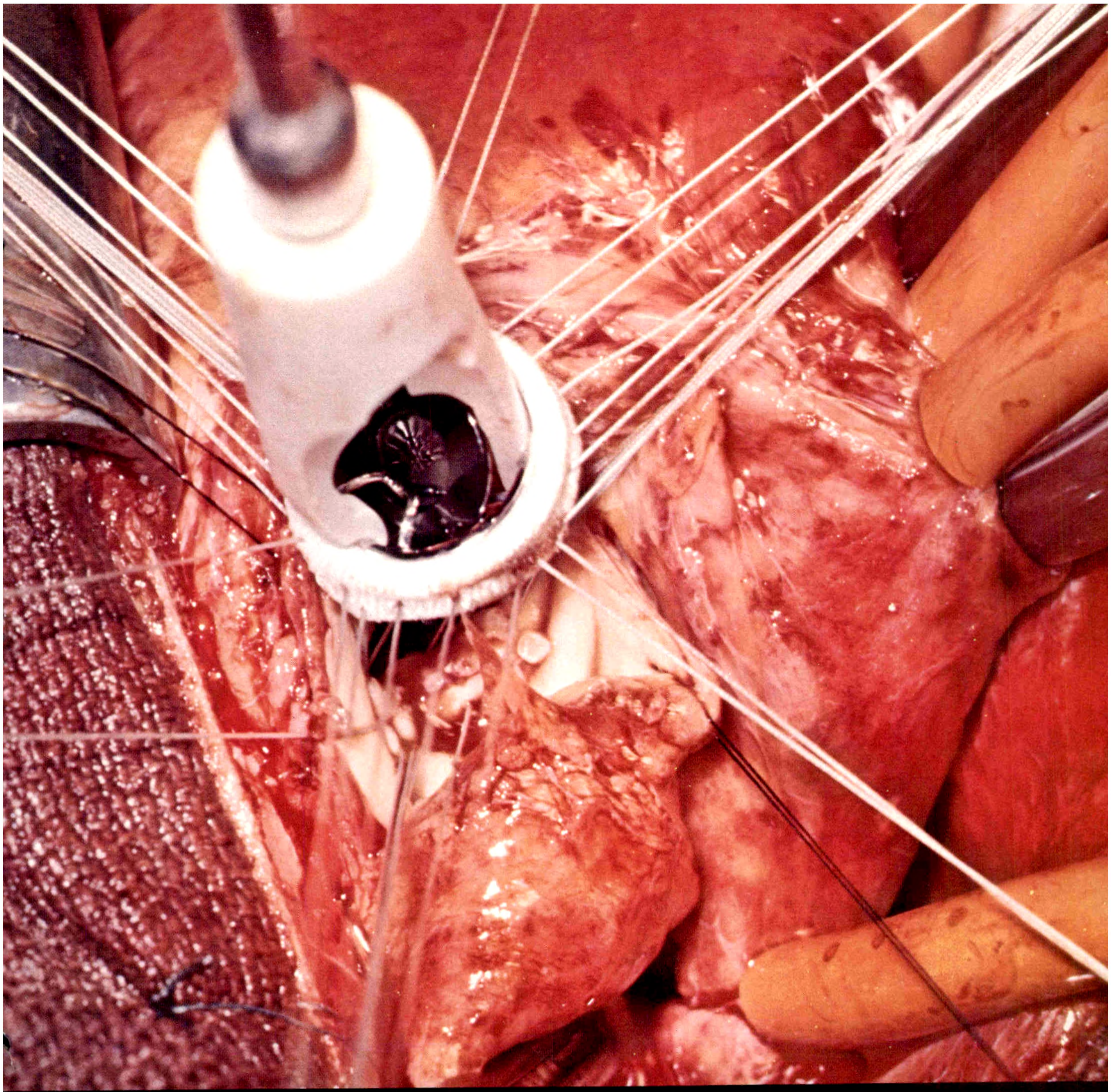
It's vitally important that effective treatment of bacterial invasion begin as soon as possible. If you suspect the presence of staph and must begin therapy before definitive culture results are known, Injection Unipen® (nafcillin sodium)† is a particularly suitable agen

Appropriate specimens fo
studies to determine the caus
and their susceptibility to naf
taken prior to the first dose o
those studies subsequently in
than penicillinase-producing
to nafcillin, discontinue it anc
priate antibiotic.

Rapid penetration
Unipen appears rapidly in pla
intramuscular administration
in high concentrations and di
pericardial and synovial fluid



"On call" capability
Reconstitutes in less than 60 seconds. Remains stable for 24 hours.‡

Follow-up therapy: oral
Unipen (nafcillin sodium) is available in tablets, capsules, and oral solution as well as the parenteral form. The injectable form should be used initially in severe infections. And as soon as the clinical condition warrants, oral forms of Unipen allow you to continue antistaph therapy with the same antibiotic in a form more convenient to patients.

INJECTION AND ORAL
UNIPEN®
(nafcillin sodium)
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See important information on next page. ▶

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Informed Consent: Recall by Patients Tested Postoperatively

George Robinson, M.D., and Avraham Merav, M.D.

ABSTRACT **When tested for recall between 4 and 6 months following operation, 20 patients failed to remember accurately major portions of their informed consent interview. Documentation of the details of consent in the clinical record is considered advisable.**

It is the patient's right to determine whether he will or will not undergo surgical treatment, and it is the responsibility of the surgeon to provide information for the patient so that he can make an intelligent decision based upon comprehension of the intended procedure. Variations in the standards of adequacy of such information and recent changes in laws across our nation make judgments on the details and validity of informed consent very difficult [1]. Several recent legal decisions have transferred evaluation of the adequacy of informed consent from physicians to the jury, and it is now the latter who may decide whether adequate information has been supplied to permit the patient to make a sensible decision with respect to treatment. Certainly, when he is considering whether to undergo a major operation the patient requires information as to the possibility of death or injuries from potential complications. He is also entitled to an expert evaluation of the alternatives to surgical treatment.

The extent to which physicians must inform patients has recently been determined to be that information which is material to the decision-making process. Information regarding complex technological methods, surgical procedures, and prosthetic devices is difficult to transmit to the wide spectrum of patients. Total comprehension by patients, even those with a medical background, may be impossible to achieve, yet the physician is duty bound to inform. By training and experience, the surgeon is accustomed to rendering a prospective analysis of a clinical problem and to evaluating methods alternative to surgery. He should therefore be able to present this material to the patient in a comprehensible form. Documentation of this transmittal of information in the patient's clinical records has been shown to be desirable.

We have made a conscientious effort to obtain fully informed consent from all our patients undergoing cardiac procedures. Since January, 1975, tape recordings have been made of the informed consent conversations; these recordings were made with the knowledge and permission of the patients. In a carefully structured but informal session one or two days prior to operation, the elements of informed consent were systematically covered in considerable detail.

The outline of information included in each interview was as follows:

1. Diagnosis and nature of the illness
2. Proposed operation, surgical techniques to be employed, and prosthetic devices to be used (if applicable)
3. Risk of death resulting from the operative procedure
4. Potential complications of operation and prosthetic devices (if applicable)
5. Benefits of the proposed operative procedure
6. Alternative methods of management and their chances for failure or success
7. Acknowledgment by the patient of his understanding of all explanations and answering of questions

We were first alerted to the major loss of recall that occurs following the informed consent interview when 2 patients, both of whom were convalescing normally at ten days and six weeks after their operations, denied any recollection of the preoperative recorded interview. A formal study of recall by postoperative testing was then initiated.

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Materials and Methods

Between 4 and 6 months following operation, 20 patients were selected for reinterview to determine the capacity of each to recall the details of their informed consent interview. Each of these patients had convalesced uneventfully after a satisfactory postoperative course. Patient selection was otherwise totally random. Ages ranged between 35 and 66 years, with a mean age of 52 years. Nine patients had undergone operation for atherosclerotic heart disease, and 11 patients had been operated upon for acquired valvular heart disease. Recordings were also made at the time of the second interview. All patients had been hospitalized one or more times previously for diagnostic or therapeutic purposes, and none had had their operations performed as emergency procedures.

All informed consent interviews were conducted by one author (G. R.), and all reinterviews were conducted by the second author (A. M.). Before reinterview the original tape recording was replayed, and a chart of the points discussed in each category of informed consent was prepared for rapid reference. At the reinterview each category of the consent procedure was reviewed twice to determine the patient's ability to recall. *Primary recall* was the response to general questions in each category of consent (1 to 6). Questions asked during the primary recall portion of the reinterview were identical for all patients. An effort was made to avoid suggesting responses. The questions were:

Do you remember having an interview with Dr. Robinson before your operation?
Tell me what you remember of the interview.
What were you told about what was wrong with you—the diagnosis?
What were you told about the operation to be performed?
Were you told of risks or dangers associated with the operation?
Were any of the possible complications associated with the operation discussed? What were they?
Were you told in what way the operation would help you?
Were you told about methods of treatment other than operation?

Following this, the itemized list of topics from the prepared chart was then reviewed with the patient. The patient was asked if each item had been discussed originally and, if affirmative, what the substance of the conversation was. The response of the patient to questions regarding specific items known to have been discussed in the original interview was designated *secondary recall*. Suggestions of correct responses were unavoidable in testing for secondary recall.

Accuracy of primary and secondary recall was then graded 0 to 100% in each of the categories 1 through 6 of the informed consent interview. If there was no recall of a category having been discussed, a score of 0 was given. Partial scores were awarded according to the degree of recall in each category. No deductions were made for denial, fabrication, or errors of attribution.

Results

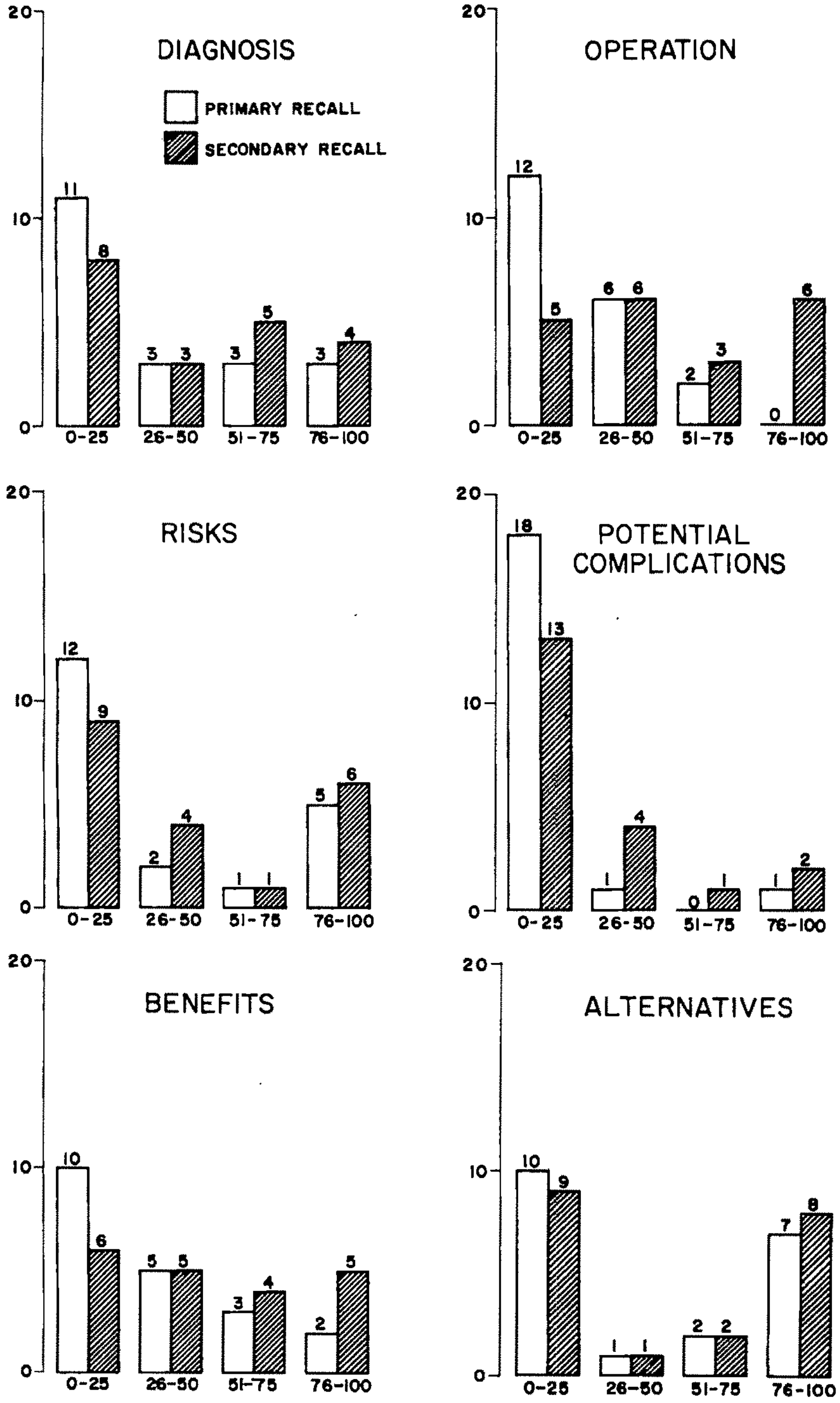
Findings upon reinterview indicated generally poor retention in all categories of informed consent information. The Table indicates the aver-

Recall of Informed Consent Interview by 20 Patients 4 to 6 Months Postoperatively

Category of Informed Consent Information	% Primary Recall	% Secondary Recall
1. Diagnosis and nature of illness	33	46
2. Proposed operation	26	51
3. Risks of the operative procedure	35	42
4. Potential complications	10	23
5. Benefits of the proposed operation	29	47
6. Alternative methods of management	43	43
Average	29	42

age scores achieved by 20 patients reinterviewed in each of the 6 categories. The poorest scores were achieved in the single category of potential complications: there was 10% primary recall and, with the suggestion of appropriate responses, a secondary recall of 23% out of a possible 100% for this category. The average recall in all categories was 29% for primary and 42% for secondary recall. Thus, even with the influence of suggestion and a point-by-point review of every item covered in the original interview, patients could remember only 42% of the items that had been covered in the informed consent interview. The Figure illustrates the

Primary and secondary recall in each category of informed consent. Vertical axis indicates number of patients; horizontal axis indicates scores in percent.



scores achieved by percentage groups in each category and demonstrates the improvement in secondary recall. Of the 20 patients tested, 17 scored 50% or less on primary recall and 12 scored 50% or less on secondary recall. The lowest individual score achieved was 3% primary and 3% secondary recall, and the highest score achieved was 57% primary and 87% secondary recall.

Errors made by patients in the repeat interview had qualitative differences. They may be described as failure to recall; positive denial of a truth; fabrication, or the assertion of an untruth or falsehood; and errors of attribution.

Each of the 20 patients failed to recall major parts of the interview. Sixteen of the 20 patients positively denied that certain major items had been discussed at all. Of these 16 patients who made positive denials, 13 denied having been informed on multiple (maximum of eight) significant items of information. After failure to recall and denial, the next most common error was fabrication, or the assertion of an untruth or falsehood. This was present to a significant degree in 13 of the 20 patients reinterviewed. A common error (and one that is quite understandable) was attribution of information gathered from other sources to the informed consent interview.

Two patients voluntarily complained that the preoperative interviews were very brief, inferring that they were not informative. One of these stated that "all he did was lift up my shirt, put a stethoscope on my heart, and that was it." The recorded portion alone of this informed consent conference was 24 minutes long. The second complaint about brevity of the interview came from a patient whose recording lasted 23 minutes. The unrecorded portions of each consultation visit easily exceeded 10 additional minutes.

Noteworthy was a significant difference in the self-assurance with which patients responded to questions in reinterviews. The quality of responses to questions often indicated some doubt or lack of certainty. Three patients were considered to have a quality of response that indicated near total self-assurance in being correct in the details of recall. The poorest score of all 20 patients reinterviewed was achieved by a patient who responded authoritatively and expressed no doubts regarding his recollections. Two other patients, who scored fifteenth and seventeenth, respectively, also had the same quality of response: they were frequently in error but never in doubt.

Comment

Despite meticulous attention to detail by the surgeon in a carefully conducted informed consent procedure, all of 20 patients tested between 4 and 6 months postoperatively failed to recall accurately what had transpired at their interview. The informed consent had been given in a simple, direct, and uncomplicated manner in the form of a dialog between the patient and the surgeon. There were repeated instances in each conversation in which the patient was asked if he understood the explanations, and questions were answered as they arose. We believe, therefore, that all patients completely understood the information imparted and that they gave a truly informed consent to their operations. Noteworthy is the fact that the patients studied had been educated by their previous experience with their disease; all had chronic heart disease and had been hospitalized many times for diagnostic and therapeutic procedures. This study calls attention to the fact that, while these patients were well informed and comprehended their situations prior to operation, they subsequently forgot most of what they had understood and made other qualitative errors in their attempts to recall the consent interview. We believe it is essential to document in some way the details of informed consent so that it becomes a permanent part of the clinical record, since memory of the event is unreliable.

Reference

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In Vivo Evaluation of the Lillehei-Kaster Heart Valve Prosthesis

U. Sigwart, M.D., H. Schmidt, M.D.,
U. Gleichmann, M.D., and H. G. Borst, M.D.

ABSTRACT **In vivo evaluation of the Lillehei-Kaster heart valve prosthesis was performed in 28 patients; 22 had undergone aortic valve replacement and 6 had had mitral valve replacement.**

Mean pressure gradients ranged from 6 to 53 mm Hg in aortic prostheses; valve area varied from 0.83 to 2.9 cm^2. The maximum opening angle of 80 degrees was never reached in this group of patients; opening angles ranged from 57 to 74 degrees without evidence of disc malfunction. There was no correlation between the ratio of effective to geometric valve area and the degree of opening of the disc occluder.

Similar results were found in the mitral valve group. Gradients ranged from 6.0 to 12.5 mm Hg and valve area from 1.6 to 2.2 cm^2. The maximum opening angle was 59 to 63 degrees.

It is concluded that incomplete opening of the disc occluder in pivoting-disc valves is not necessarily a sign of disc malfunction. Lillehei-Kaster valves smaller than 18 mm in internal diameter should be avoided in adults, and outflow aortoplasty for implantation of a larger prosthesis should be used in patients who have a narrow aortic root.

A serious challenge has been introduced to the traditional ball-valve cardiac prosthesis by the increasingly used tilting-disc devices. The pivoting-disc prostheses were developed in an effort to minimize obstruction to flow and turbulence. Cloth-covered ball valves have become less frequently implanted [1] since it became clear that cloth wear and higher obstruction to flow are drawbacks that have to be weighed against the advantage of a lower incidence of thromboembolism. Although bare-strut ball valves are experiencing some revival, the popularity of the tilting-disc prosthesis is still increasing rapidly. The first and still most frequently used tilting-disc heart valve is the Björk-Shiley prosthesis, which was introduced in 1969. At that time, the Lillehei-Kaster prosthetic valve was undergoing preclinical investigation. Currently an estimated 10,000 Lillehei-Kaster valve prostheses are implanted annually.*

Although the central-flow valves appeared to be superior to the caged-ball or low-profile disc prostheses in extensive hydrodynamic laboratory investigations [6], no systematic in vivo measurements of the properties of this particular valve type have been published. The present investigation is concerned with the in vivo hemodynamic properties of the Lillehei-Kaster valve prosthesis with regard to obstruction to flow, flow patterns, and disc motion analysis.

Clinical Material and Methods

During a nine-month period from November, 1974, to July, 1975, 28 patients were studied from 3 to 24 weeks following operation; 22 were recatheterized after aortic valve replacement and 6 after mitral valve replacement (Table 1). Eight patients had been operated on for aortic stenosis with aortic insufficiency, 9 for aortic stenosis, and 5 for aortic incompetence; mitral valve replacement was carried out 3 times for mitral incompetence and 3 times for combined lesions with stenosis and insufficiency. There were 10 women and 18 men, the average age being 49 ± 9 years in the aortic valve group and 55 ± 4 years in the mitral valve group. Three patients within the aortic valve group (G. M., H. W., H. A.) presented additional evidence of coronary heart disease; 1 had a history of myocardial infarction (H. A.).

Most patients in this study were examined by cardiac catheterization preoperatively and postoperatively in the same setting. Catheterizations were performed in the postabsorptive state

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*Kaster RL: Personal communication, 1975.

Table 1. Preoperative and Postoperative Catheterization Data in 28 Patients Receiving Lillehei-Kaster

Patient, Age, & Sex	Valve Size (mm)	Heart Rate (min^{-1})			Cardiac Index (L/min/m^2)			Hgb (gm/100 ml)		LVP, S/EDP (mm Hg)		
		Rest		Exercise (postop)	Rest		Exercise (postop)			Rest		Exercise (postop)
		Preop	Postop		Preop	Postop		Preop	Postop	Preop	Postop	
Aortic valve replacement												
G. A., 52, F	14A	...	SR 72	...	...	3.1	...	...	12.1	...	162/20	...
S. F., 59, F	14A	SR 76	SR 60	...	2.9	2.6	...	14.1	13.8	285/30	181/14	...
G. M., 64, F	16A	SR 78	SR 71	...	2.4	3.3	...	12.0	12.5	200/7	202/21	...
H. I., 34, F	16A	SR 65	SR 85	SR 125	3.3	3.7	5.1	12.0	12.8	155/19	170/14	195/15
H. W., 52, M	16A	SR 75	AR 83	SR 105	2.8	2.6	4.2	16.4	16.0	170/8	155/10	200/23
J. H., 44, M	16A	SR 89	SR 70	SR 107	3.2	3.6	4.5	17.5	15.3	262/54	150/21	172/33
K. H., 59, F	16A	SR 82	SR 83	...	2.9	3.4	...	11.3	11.3	220/14	155/14	...
K. L., 41, M	16A	SR ...	SR 69	SR 100	...	3.1	5.2	...	15.8	...	140/7	145/20
M. K., 49, M	16A	SR 90	SR 116	SR 145	2.9	3.0	3.3	13.9	14.2	230/15	162/14	205/15
S. E., 38, F	16A	SR 70	SR 84	...	...	5.6	...	...	9.1	...	175/16	...
S. P., 50, M	16A	AF 65	SR 91	SR 105	2.6	3.4	4.2	16.7	14.0	280/30	170/17	195/25
S. A., 30, M	16A	SR 105	SR 101	SR 130	2.8	3.2	4.9	...	10.3	140/7	165/7	200/9
Z. E., 53, M	18A	AF 96	SR 79	...	2.1	4.0	...	13.3	12.9	120/27	130/10	...
L. E., 62, F	18A	SR 72	SR 100	...	3.8	3.6	...	14.1	12.5	265/25	135/7	...
H. A., 48, M	18A	SR 75	...	...	2.7	3.3	...	16.9	...	235/17	185/15	...
S. H., 47, M	20A	SR 77	SR 91	SR 115	3.1	3.2	4.3	16.3	12.9	195/18	123/13	160/23
M. E., 35, M	20A	...	SR 72	...	...	3.0	...	...	14.7	135/16	...	...
T. K., 52, M	20A	SR 73	SR 96	...	4.4	3.1	...	14.5	13.8	155/16	145/6	...
L. W., 51, M	22A	SR 70	SR 71	SR 98	3.1	3.6	...	13.3	13.8	195/35	160/11	...
B. W., 49, M	22A	SR 86	SR 100	SR 113	3.6	3.2	4.8	16.2	12.2	135/15	129/10	158/24
W. L., 45, F	25A	SR 79	SR 73	SR 102	3.5	4.1	4.6	14.2	12.9	112/	120/10	155/14
W. R., 59, M	25A	SR 60	AF 67	...	2.2	2.3	...	15.2	15.2	150/16	137/8	...
Mitral valve replacement												
M. G., 51, M	20M	SR 64	SR 75	SR 115	2.5	3.3	...	13.7	15.1	138/14	125/13	180/16
S.G., 62, M	20M	JR 57	SR 84	...	2.2	2.4	...	13.6	12.0	137/21	145/13	...
H. J., 57, F	22M	SR 110	SR 75	SR 110	2.4	3.4	4.9	15.7	14.2	.../14	130/5	180/10
M. H., 51, M	22M	SR 90	SR 63	SR 94	2.6	3.6	4.2	15.6	13.8	140/46	125/20	135/25
K. M., 52, F	22M	AF 103	AF 69	...	1.8	2.4	...	14.0	14.6	120/6	123/11	...
H. K., 57, M	22M	AF 105	SR 92	...	2.0	3.0	...	16.3	12.0	110/12	127/5	...

Hgb = hemoglobin; LVP = left ventricular pressure; S/EDP = systolic/end-diastolic pressure; AoP = aortic pressure; S/DP = systolic/diastolic pressure; LAP = left atrial pressure; AVG = aortic valve gradient; AVA = aortic valve area; VA = valve area; SR = sinus rhythm; AF = atrial fibrillation; JR = junctional rhythm; AS = aortic stenosis; IHD = ischemic heart disease; AI = aortic insufficiency; a = a wave; v = v wave; m = mean; PAP = pulmonary artery pressure; MVG = mitral valve gradient; MVA = mitral valve area; MS = mitral stenosis; MI = mitral insufficiency.

after mild sedation (diazepam, 10 mg orally). Flow measurements and determination of valve gradients were done simultaneously. By the percutaneous femoral route a 7F Swan-Ganz thermodilution catheter was advanced to the pulmonary artery; a 7F Cordis Ducor Pigtail catheter was inserted into the aortic root (or the left ventricle in the case of mitral valve disease), and an 8F Brockenbrough catheter was introduced transseptally into the left atrium (or into the left ventricle in aortic valve disease). Cardiac output was determined by the thermodilution method with a small analog calculating unit.* There was good agreement between this method and manual calculations as well as with determination of cardiac output by the Fick method.

Pressure measurements from the fluid-filled catheter system were taken through Elema transducers and recorded simultaneously (Fig 1) on a Mingograph eight-channel ink-jet re-

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Aortic or Mitral Valve Prostheses

AoP, S/DP (mm Hg)			Mean LAP (mm Hg)		Mean AVG (mm Hg)			AVA (cm²)		πr^2 Meas. VA (cm²)	Effective VA (%)	Degree of Opening Angle	Diagnosis
Rest		Exercise (postop)			Rest		Exercise (postop)						
Preop	Postop		Preop	Postop	Preop	Postop		Preop	Postop				
. . .	137/75	. . .	. . .	19	. . .	32	. . .	. . .	0.97	1.54	62.9	66	Severe AS
115/75	178/80	. . .	8	4	. . .	28	. . .	. . .	0.91	1.54	59.0	68	Severe AS
107/73	195/95	. . .	7	11	81	16.2	. . .	0.43	1.56	2.01	77.6	. . .	Severe AS, mild IHD
155/50	163/100	175/105	20	12	. . .	30.0	46.0	. . .	1.06	2.01	52.7	. . .	Marked AI
110/70	145/75	185/75	6	6	61	23.5	. . .	0.7	1.17	2.01	58.2	. . .	Marked AS, mild IHD
146/89	120/80	145/85	24	11	114	38	52	0.8	1.22	2.01	60.6	. . .	Marked AS, mild IHD
105/50	110/65	. . .	9	10	94	46.5	. . .	0.45	0.83	2.01	41.2	. . .	Marked AS, mild IHD
. . .	120/75	110/70	. . .	6	. . .	24.5	46.0	. . .	1.32	2.01	65.6	62.0	Marked AS
135/65	125/75	140/85	11	8	87	53	. . .	0.48	0.92	2.01	45.7	. . .	Marked AS
. . .	140/70	. . .	. . .	17	. . .	20.4	. . .	. . .	1.4	2.01	69.6	56.0	Moderate AS + AI
115/60	. . .	145/85	32	12	112	. . .	46.5	0.5	1.4	2.01	69.6	. . .	Marked to severe AS, mild AI
140/55	135/80	170/80	10	3	. . .	41.8	51.8	. . .	1.22	2.01	60.6	. . .	Moderate AI
115/45	120/62	. . .	33	7	40.3	24.5	. . .	1.07	1.65	2.54	64.9	. . .	Marked AS, moderate AI
170/100	123/65	. . .	20	5	93.0	19.0	. . .	0.75	1.68	2.54	66.1	. . .	Marked to severe AS
181/104	176/107	. . .	10	6	69.0	21.7	. . .	0.7	1.36	2.54	53.5	57	AS, IHD
137/80	123/75	140/87	12	8	69.0	13.5	. . .	0.8	1.84	3.14	58.5	. . .	Marked AS
. . .	135/75	. . .	. . .	8	. . .	13.5	. . .	. . .	2.2	3.14	70.0	65	Marked AI
135/50	137/79	. . .	19	8	52	15.4	. . .	1.1	1.62	3.14	51.5	61	Marked AS + AI
195/55	150/87	. . .	16	8	. . .	7	. . .	. . .	2.89	3.80	76.0	. . .	Severe AI
120/60	128/88	157/94	13	7	19	6	. . .	1.5	2.41	3.80	63.4	67	Moderate AS, marked AI
112/	120/70	155/80	6	7	. . .	6.8	18.4	. . .	2.92	4.91	59.5	. . .	Marked AI
108/50	136/51	. . .	7	9	52	6.0	. . .	0.6	2.6	4.91	53.0	74	Severe AS, mild AI

LAP (mmHg) (a/v/m)			Mean PAP (mm Hg)		Mean MVG (mm Hg)			MVA (cm²)					
Rest		Exercise (postop)			Rest		Exercise (Postop)						
Preop	Postop		Preop	Postop	Preop	Postop		Preop	Postop				
30/35/25	21/30/21	. . .	30	24	14.5	12.5	. . .	1.21	1.61	3.14	51.2	. . .	Severe MS + MI
. . ./70/30	18/40/21	. . .	. . .	34	. . .	7.6	. . .	. . .	1.98	3.14	63.1	. . .	Severe MI
34/39/31	15/24/16	24/33/25	38	20	15.2	7.9	14.0	0.69	1.84	3.80	48.4	. . .	Moderate MS + MI
41/69/47	20/24/16	32/50/27	65	50	. . .	8.5	. . .	. . .	2.19	3.80	57.6	. . .	Marked MI
. . ./23/17	. . ./21/13	. . .	45	26	12	6.0	. . .	0.58	1.75	3.80	46.1	59	Marked to severe MS, mild MI
. . ./39/20	11/9/7	. . .	25	19	. . .	10	. . .	. . .	1.56	3.80	40.8	63	Severe MI

corder* and an optical writer.† Valve gradients were obtained by integration of the pressure gradient after correction for specific delay due to different time constants in the catheter-manometer systems. The diastolic filling period was defined from the point of intercept between the left atrial and left ventricular curve in the descending slope of the "v" wave of the left atrium to the first intercept appearing after mid-diastole; a similar approach was used for calculation of the systolic ejection period.

The valve orifices were determined by the Gorlin formula, using an orifice coefficient of 1.0 [5] for the aortic valve and 0.85 [2] for the mitral valve. Measurements were taken in all patients at rest as well as in 7 patients postoperatively during exercise using an electrically braked bicycle ergometer.* Angiography was performed after the hemodynamic measurements had been completed. In all patients biplane left ventricular angiograms were taken during injection of 35 to 45 ml of Renografin 76. In patients undergoing aortic valve replacement, aortic root injections were also obtained. No complications occurred.

Motion analysis of the moving disc of the valve prosthesis was performed independently from the cardiac catheterization through

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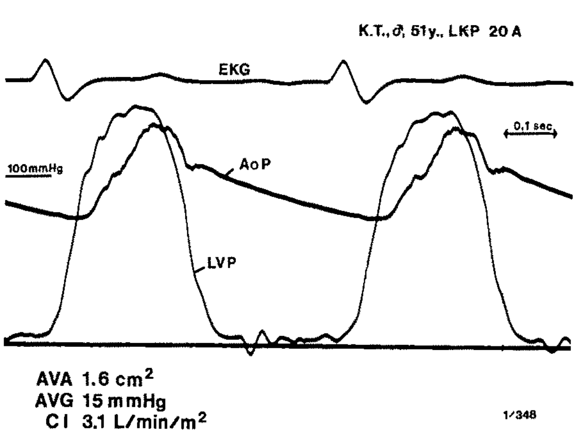


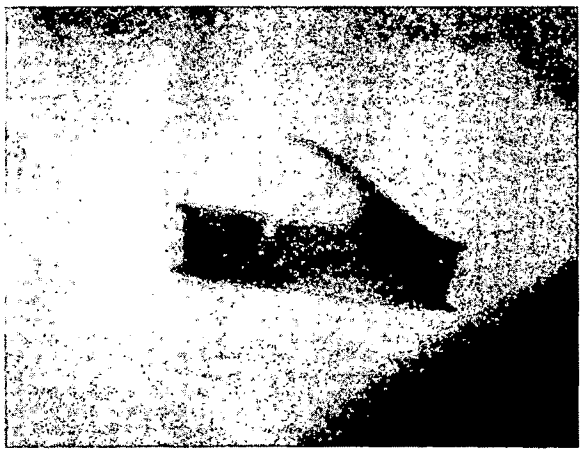
Fig 1. Original tracing of simultaneously recorded left ventricular pressure (LVP), *aortic pressure* (AoP), *and electrocardiogram from a patient with a Lillehei-Kaster aortic valve prosthesis (20 mm internal diameter).* (AVA = *aortic valve area;* AVG = *aortic valve gradient;* CI = *cardiac index.)*

fluoroscopy and high-speed cine filming. Employing a Siemens Cardoscop U with a 17 to 24 H duplex high-resolution image intensifier, the patient was turned in such a manner that the chordal axis, about which the disc can pivot within the titanium housing, was parallel to the central x-ray beam (Fig 2). This pattern allows easy recognition of the opening angle of the disc without the use of contrast medium. Films were taken at a speed of 150 frames per second.

Hemodynamic Results

A synopsis of the hemodynamic data is depicted in Table 1. The heart rate did not change significantly after operation in either the aortic or the mitral valve group.

Fig 2. Roentgenographic appearance of a Lillehei-Kaster valve prosthesis taken from a 35 mm cine film during systole; the disc is clearly visible in the open position.



Aortic Valves

In all patients who were operated on for aortic stenosis there was a significant decrease in pressure gradients and increase in valve area after implantation of the Lillehei-Kaster valve ($p < 0.001$). In these patients the average mean valve gradient was 73 ± 28 mm Hg preoperatively and 23 ± 13 mm Hg postoperatively; with exercise the postoperative valve gradient increased to 43 ± 13 mm Hg. In the entire aortic valve group the mean resting cardiac index was 3.0 ± 0.6 L/min/m² preoperatively and 3.3 ± 0.7 L/min/m² after operation ($p > 0.05$). The postoperatively measured cardiac output with exercise increased to 4.5 ± 0.6 L/min/m². Aortic valve prostheses with an internal diameter of 16 mm or less showed strikingly larger mean pressure gradients (32 ± 11.6 mm Hg) at rest as compared with the larger valves (13 ± 6.9 mm Hg). The mean aortic valve areas with the corresponding internal diameters and geometric valve areas (πr^2 − 20% for space occupied by the disc in the fully open position [9]) are depicted in Table 2. There is a 76% average ratio between the hemodynamically effective valve area and the geometric valve orifice.

Except for a patient with mechanical obstruction to opening due to tissue ingrowth or thrombosis, who was not included in the study, there was no significant correlation between the ratio of geometric to effective orifice area and the maximum opening angle in systole (Fig 3).

Table 2. Effective and Geometric Valve Areas of Lillehei-Kaster Aortic Prostheses

Size (mm)	Valve Area (mm²)	Absolute Geometric Valve Area (mm²)	Ratio
14	0.94	1.23	0.76
16	1.21	1.61	0.75
18	1.56	2.03	0.77
20	1.89	2.51	0.75
22	2.65	3.04	0.87
25	2.76	3.93	0.70

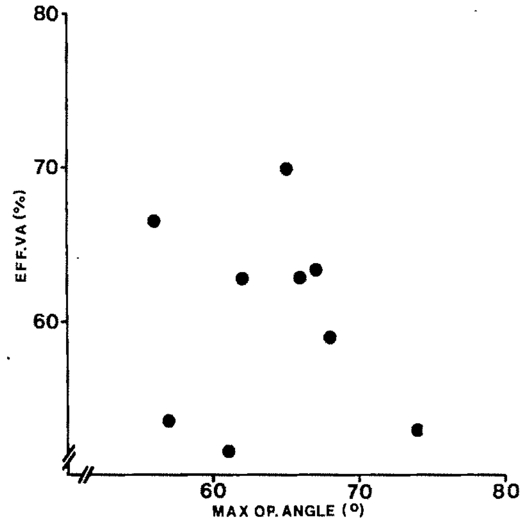


Fig 3. No correlation was seen between maximum measured opening angle of the disc during systole and a ratio of measured to geometric valve area in 9 patients with the Lillehei-Kaster prosthesis in the aortic position. (EFF.VA = *effective valve area.)*

Hemoglobin was significantly higher preoperatively (14.6 ± 1.9 mg/100 ml) than postoperatively (13.2 ± 1.7 mg/100 ml; $p < 0.05$). Left ventricular end-diastolic pressure dropped from 21 ± 12 to 13 ± 5 mm Hg ($p < 0.05$).

Mitral Valves

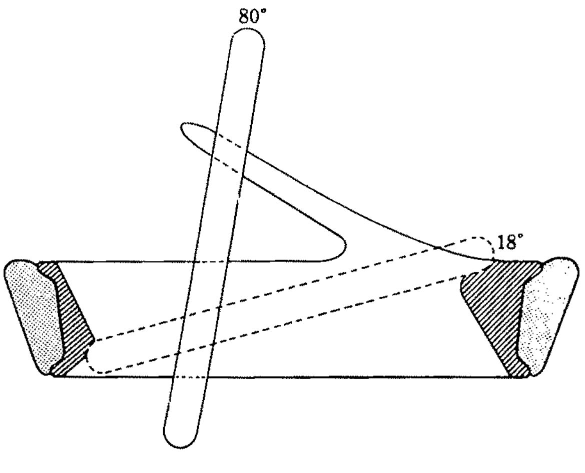
The mean cardiac index increased from a preoperative value of 2.3 ± 0.3 L/min/m^2 to 3.0 ± 0.5 L/min/m^2 postoperatively. The mean pressure gradient in patients with mitral incompetence or combined lesions dropped from 14 ± 1.7 to 9 ± 2.2 mm Hg ($p < 0.05$). Left atrial mean pressure decreased from 28 ± 11 to 16 ± 5 mm Hg ($p < 0.05$). With exercise the pressure gradient in 1 patient increased from 8 to 14 mm Hg. The mean mitral valve orifice area at rest was 1.8 ± 0.2 cm^2. The ratio of effective to absolute geometric orifice area ($\pi r^2 - 20\%$ for space occupied by the disc in the fully open position) was 0.64.

No significant change was observed in hemoglobin before (14.8 ± 1.2 gm/100 ml) and after operation (13.6 ± 1.3 gm/100 ml). Left ventricular end-diastolic pressure dropped from 19 ± 14 to 11 ± 6 mm Hg after implantation of the valve prosthesis; this is explained by the fact that no patient was operated upon for predominant mitral stenosis.

Comment

Our particular interest was based on the hemodynamic properties of the Lillehei-Kaster prosthesis with respect to obstruction to flow and the opening angle of the valve prosthesis. It had been noted in earlier studies that all previously available prosthetic heart valves have pressure gradients that are disappointing from the clinician's standpoint [4, 13, 15]. With the appearance of the pivoting-disc prosthesis this major drawback was thought to have been largely overcome, since this valve design allows blood to flow centrally through the orifice with only minor obstruction due to incomplete opening of the disc. Recently the Björk-Shiley valve was redesigned in order to increase the opening angle from 50 to 60 degrees. The Lillehei-Kaster prosthesis is designed for an opening angle of 80 degrees (Fig 4). Lillehei and associates [9] have compared five different heart prostheses of comparable external diameters with regard to flow rate and pressure gradient at a given left ventricular pressure in vitro. Measurements were taken using a pulse duplicator with pulsating flow and simulated blood (65% glycerine and 35% saline). If one calculates valve orifice area from these data using the Gorlin formula, one finds the same range for the Lillehei-Kaster prosthesis as we did in our in vivo measurements. At a peak left ventricular pressure of 150 mm Hg the flow rate would be 4.8 L/min, producing a gradient of 25 mm Hg; at an ejection

Fig 4. Cross-section through the Lillehei-Kaster valve prosthesis [9]; the disc can tilt from 18 degrees in the closed position to 80 degrees in the open position.

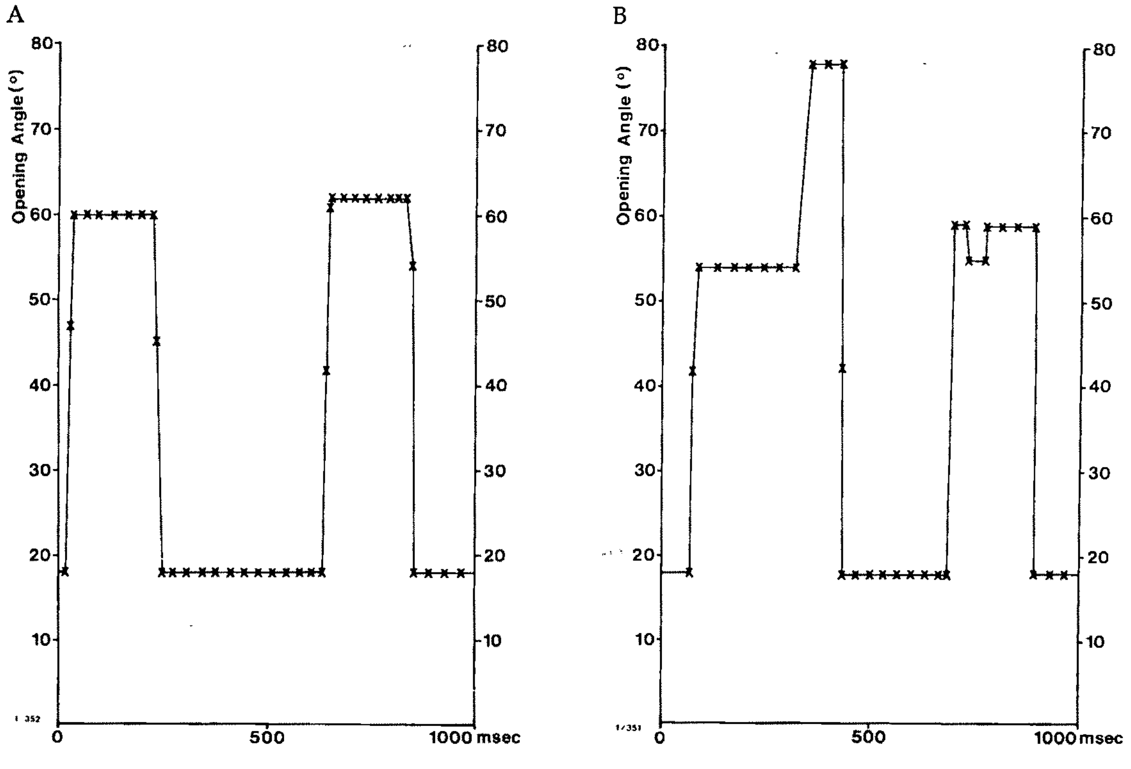


period of one-third of the cycle at 72 beats/min, this would result in an orifice area of 1.3 cm^2 for the 18 mm Lillehei-Kaster aortic prosthesis. This represents 64% of the absolute geometric orifice area, a figure which is within the same magnitude as calculated from our hemodynamic studies. With this in mind, it is difficult to believe that the orifice area determined by the hydraulic formula should be equal to or larger than the actual geometric orifice area [9].

In vitro tests comparing two types of tilting-disc valves—the Björk-Shiley and the Lillehei-Kaster—at different opening angles showed the Björk-Shiley valve to be superior in terms of obstruction to flow at low opening angles; however, at a 75 degree opening angle the Lillehei-Kaster valve was less obstructive than the Björk-Shiley valve [7]. If one assumes that the disc opens completely in every case, the Lillehei-Kaster valve would be preferable according to the in vitro tests. However, in our experience the theoretical opening angle of 80 degrees for the Lillehei-Kaster valve has not been reached in vivo (see Table 1). Surprisingly enough, the disc stops its opening movement at a fixed angle that is fairly stable from beat to beat in a single individual (Fig 5A). Only in patients with atrial fibrillation can it be observed that at high filming rates the disc opens for just a few milliseconds to more than the average degree (Fig 5B). The reason for this is unknown, since in vitro tests have not revealed this phenomenon at all; on the contrary, there still appears to be an opening momentum at the opening angle of 80 degrees, so one would expect the disc to open completely in most instances.

Since the pivoting axis is located eccentrically, it was estimated in laboratory tests that flow through the larger opening amounts to four-fifths of the entire valve flow. According to our

Fig 5. (A) Disc motion analysis at a speed of 150 frames per second in a patient (L. K.) in sinus rhythm shows little beat-to-beat variation with regard to maximum measured opening angle. The disc remains in the same position throughout the ejection period. (B) In atrial fibrillation a striking variation of the systolic opening angle can be observed in selected patients. The first systole shows a late, brief increase in the opening angle to 77 degrees. This phenomenon was seen only once; it demonstrates the absence of a mechanical stop. The patient (H. K.) returned to sinus rhythm before hemodynamic studies were performed (see Table 1).



experience in vivo, this observation is correct. After contrast medium is injected into the aortic root, rapid washout can be observed only on the larger opening side of the tilting-disc valve, whereas there is turbulence and persistence of contrast medium behind the disc, resulting in delayed washout. This turbulence might be the reason why the valve opens incompletely, for no mechanical stop could be detected. Since the Björk-Shiley and Lillehei-Kaster valve prostheses open to a similar degree, the major advantage of the flow characteristics of the Lillehei-Kaster valve at large opening angles would be abolished.

In accordance with others, we found striking clinical improvement after implantation of aortic or mitral Lillehei-Kaster valve prostheses [8, 10, 11]. Dyspnea was reduced in all patients to at least one stage lower of the New York Heart Association's dyspnea classification. Hemolysis has never been a problem in this series, as estimated by serum hemoglobin and lactic dehydrogenase determinations. Mild LDH elevation was seen in 2 patients; this incidence is similar to the observation of others [12]. In a preliminary study of the incidence of thromboembolism in 125 patients undergoing aortic valve replacement without the use of anticoagulants, Dalichau and co-workers [3] did not find any significant difference between the Lillehei-Kaster and other valve designs. Our investigation was not focused on thromboembolic disorders due to prosthetic valves, but the short-term results confirmed the previous findings.

From hemodynamic and clinical data the Lillehei-Kaster prosthesis appears to compare favorably with other valve designs. However, remarkable pressure gradients are still seen with the smaller valves, resulting in moderate to marked stenosis. In patients with a narrow aortic root, outflow annuloplasty should be considered to achieve gratifying long-term results. The technical feasibility of this procedure has been demonstrated [14]. We propose that prosthetic heart valves of at least 18 mm internal diameter be used in the aortic position in adults in order to minimize prosthesis-induced stenosis. A prosthesis of reasonable size can be implanted in most instances even without operative enlargement of the valve ring.

Early postoperative fluoroscopic control studies should be done after each valve replacement in order to study the individual motion pattern of the movable part; follow-up control tests can reveal any dysfunction easily and noninvasively. Incomplete opening appears to be the rule with the Lillehei-Kaster prosthesis and is no indication for reoperation unless the degree of opening changes significantly and there is evidence of additional obstruction to flow.

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Aortic Valve Replacement with the Hancock Porcine Xenograft

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and John J. Collins, Jr., M.D.

ABSTRACT **The Hancock porcine xenograft stabilized with the glutaraldehyde process was used for isolated aortic valve replacement in 71 patients from March, 1972, to July, 1975. Aortic stenosis was the primary diagnosis in 52 patients and aortic insufficiency in 19. There were 52 men and 19 women ranging in age from 18 to 82 years; 14 patients were older than 70 years. One patient was in Functional Class II, 50 in Class III, and 20 in Class IV preoperatively. Seventy-three patients undergoing Björk-Shiley aortic valve replacement during the same period are presented for comparison.**

The operative mortality was 3% (2 of the 71 patients); 4 of the remaining 69 patients (6%) died in the late postoperative period. No patient was placed on anticoagulation during the postoperative course, and there was 1 postoperative embolus in a patient with chronic atrial fibrillation (1.4%). With a mean follow-up period of 17 months, 60 patients are now in Functional Class I, 4 in Class II, and 1 in Class III. Seven patients have had transvalvular gradients and effective valve areas measured postoperatively that ranged from 32 to 5 mm Hg and 0.9 to 2.9 cm^2 in 21 through 25 mm (OD) sizes.

Thromboembolic phenomena are not often associated with the natural history of acquired or congenital aortic valve disease except in advanced cases in which the cardiac output is extremely low [7, 15]. Therefore, any prosthesis that is used to replace the diseased aortic valve should have as one of its primary requirements a low potential for systemic arterial embolization. No prosthetic valve yet developed can be utilized in the aortic position without the threat of thromboembolism even with anticoagulation, which carries its own morbidity and mortality [10]. Biological tissue valves, either fresh or preserved, have shown a low incidence of thromboembolism without anticoagulation, but questions of durability and logistical problems have prevented their widespread use [9].

This study reviews our experience with the Hancock porcine xenograft aortic valve preserved with the stabilized glutaraldehyde process and compares it with concurrent experience using the Björk-Shiley tilting-disc prosthetic valve.

Materials and Methods

From March, 1972, until July 1, 1975, the Hancock porcine xenograft aortic valve was implanted in 71 patients. A summary of the demographic data appears in Table 1. There were 52 men and 19 women ranging in age from 18 to 82 years (mean, 57 years). One patient was in Functional Class II, 50 in Class III, and 20 in Class IV. Fifty-two patients had critical aortic stenosis with a valve area of less than 1.0 cm^2; the peak systolic gradients in this group ranged from 40 to 140 mm Hg (mean, 84 mm Hg). Nineteen patients had predominant aortic regurgitation. The mean cardiac index for the entire group was 2.5 L/min/m^2 (1.1 to 5.1).

During about the same time period—July, 1972, to July, 1975—73 patients underwent implantation of the Björk-Shiley tilting-disc prosthetic aortic valve with the Pyrolite disc occluder. In this group (see Table 1) there were 28 men and 45 women ranging in age from 22 to 82 years (mean, 61 years). Fifty-four patients were in Functional Class III and 19 in Class IV. Sixty-two patients with critical aortic stenosis had gradients of 40 to 184 mm Hg (mean, 84); 11 patients had predominant aortic regurgitation.

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We would like to acknowledge the statistical analyses done by Ms. Caryl Boyden, Department of Surgery, and the postoperative cardiac catheterizations performed by Dr. William Grossman, Chief, Cardiac Catheterization Laboratory, Peter Bent Brigham Hospital.

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Table 1. Data on Patients Having Aortic Valve Replacement, 1972–1976

Factor	Hancock Valve	Björk-Shiley Valve
No. of patients	71	73
Male/female	52/19	28/45
Age (yr)	18–82, $\overline{57}$	22–82, $\overline{61}$
No. with stenosis/insufficiency	52/19	62/11
Atrioventricular gradient (mm Hg)	40–140, $\overline{84}$	40–184, $\overline{84}$
Cardiac index (L/min/m^2)	1.1–5.1, $\overline{2.5}$	1.1–3.6, $\overline{2.5}$

The mean cardiac index for the entire group was 2.5 L/min/m^2 (1.1 to 3.6).

Additional operative procedures were performed on some patients in both groups during aortic valve replacement. In the Hancock valve group 15 patients (21%) had other procedures: 7 had coronary artery bypass, 3 had resection and grafting of ascending aortic aneurysms, and 5 had mitral commissurotomy. In the Björk-Shiley group 14 had other procedures: 8 had coronary bypass and 6 underwent resection of ascending aortic aneurysms.

Operations were performed using cardiopulmonary bypass at physiological flow rates with a disposable bubble oxygenator, a roller pump, and moderate systemic hypothermia (30°C). In all patients, the aorta was cross-clamped and the heart was protected by local cardiac hypothermia [5]. The cardiac ischemia time was 48 to 100 minutes (mean, 65 minutes) in the porcine valve group and 42 to 120 (mean, 72 minutes) in the Björk-Shiley group. Both porcine and prosthetic valves were selected to fit precisely on the basis of the diameter of the aortic annulus (Fig 1).

The Björk-Shiley valve was generally used in patients whose annulus size was 19 or 21 mm (mean, 21 mm) and in some patients for whom Hancock valves of the proper size were not available. Patients receiving the Hancock graft had a larger aortic annulus, with a mean diameter of 24 mm (OD); the majority received 23 or 25 mm valves. Long-term anticoagulation with warfarin was used in all patients receiving a Björk-Shiley disc valve; anticoagulation was not used for patients with porcine aortic valves. Late survival, functional classification, thromboembolic complications, and mechanical function of the aortic valve were determined by personal examination or direct communication with each patient as of January 1, 1976.

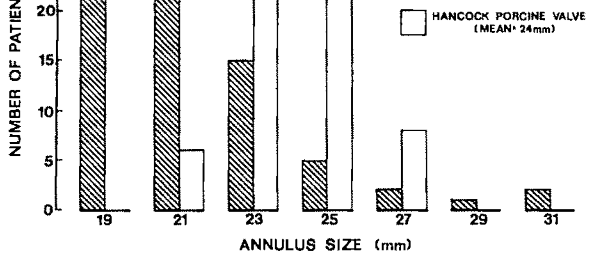


Fig 1. Valve size (in mm) for each patient in each valve group.

Actuarial curves for survival and the incidence of thromboembolism were constructed and analyzed according to the method of Cutter and Ederer [6]. In the curves for actuarial incidence of embolism, noncardiac deaths and deaths from cardiac causes other than embolism were treated as "removed for cause in interval" according to the method of Anderson and associates [1]. The statistical analyses presented in the actuarial tables were carried out according to Cochrane's combined test of significance; chi-square tests using Yates' correction were calculated at the 42-month interval [4]. Calculations were performed with the use of programs written for the Hewlett-Packard 9821-A calculator.

Seven patients underwent hemodynamic evaluation at intervals postoperatively that included calculations of left ventricular-aortic gradients and effective aortic valve area.

Results

Early and late results are summarized in Table 2. The operative mortality in the Hancock valve series was 3% (2 of the 71 patients) versus 7% (5

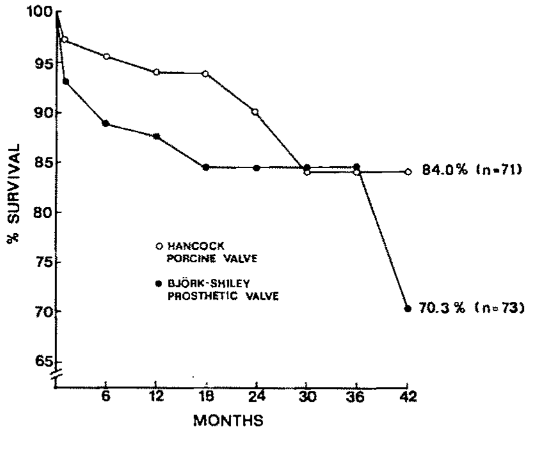
Table 2. Results following Aortic Valve Replacement

Factor	Hancock Valve	Björk-Shiley Valve
No. of patients	71	73
Operative mortality	2 (3%)	5 (7%)
Late mortality	4 (6%)	7 (10%)
Lost to follow-up	2	0
Follow-up time (mo)	6–42, $\overline{17}$	6–42, $\overline{25}$
Thromboemboli	1 (1.4%)	8 (11.8%)
Emboli/100 patient-years	1.0	6.1

of 73) in the Björk-Shiley group. Four patients died in the late postoperative period in the Hancock group (6%): 2 from infections, 1 from perivalvular leak and congestive heart failure, and 1 from a myocardial infarction. In the Björk-Shiley series there were 7 late deaths (10%): 4 patients died of thromboembolic phenomena, including 2 clotted valves; 1 patient died from myocardial infarction, 1 from arrhythmia, and 1 from carcinoma of the rectum. Actuarial survival curves for both groups of patients undergoing aortic valve replacement are shown in Figure 2. Patient survival in the Hancock valve group at 42 months was 84%, versus 70% in patients with the Björk-Shiley valve ($p = 0.2$).

Follow-up among the survivors in the Hancock valve group has been 6 to 42 months (mean, 17) versus 6 to 42 months (mean, 25) in the Björk-Shiley group. In the porcine valve group, 1 patient is in Class III, 4 are in Class II, and 60 are in Functional Class I; in the Björk-Shiley group, 54 patients are in Class I and 7 are in Class II.

Fig 2. Actuarial survival curves for patients with the Hancock porcine xenograft and Björk-Shiley valve.



There have been no Hancock porcine graft valve failures in this series from cusp rupture in the absence of infection. Valve-related complications occurred in 3 patients who suffered periprosthetic leaks necessitating reoperation; 2 had porcine valves reinserted and 1 was converted to a prosthetic valve.

There was 1 instance of thromboembolism among the 71 patients with a Hancock valve (1.4%); this occurred in a 72-year-old patient who was in chronic atrial fibrillation. In patients with the Björk-Shiley valve there have been 8 thromboembolic episodes. All were receiving anticoagulants, but 2 died from thrombosed valves when their anticoagulation regimen was altered; 2 other patients died of complications from cerebrovascular embolic disease. The actuarial analysis of the percentage of patients free from emboli at 42 months in both patient groups is shown in Figure 3: 96% of the patients with the Hancock valve and 68% of those with the Björk-Shiley prosthesis ($p = 0.07$).

Left ventricular-aortic gradients and calculated effective orifice area were determined in 7 patients who were recatheterized postoperatively (Table 3). There were 2 patients with 21 mm, 2 with 23 mm, and 3 with 25 mm (outside diameter) valves. For the 21 mm size, gradients were 10 and 32 mm Hg and effective orifice areas were 1.2 and 0.9 cm^2; for the 23 mm grafts, gradients were 10 and 30 and effective orifice areas, 1.2 and 1.1 cm^2; gradients in the 25 mm group were 20, 5, and 5 mm Hg and orifice areas were 1.3, 1.2, and 2.9 cm^2.

Comment

The results indicate that the Hancock porcine aortic valve has a very low incidence of as-

Table 3. Postoperative Hemodynamic Data after Porcine (Hancock) Aortic Valve Replacement

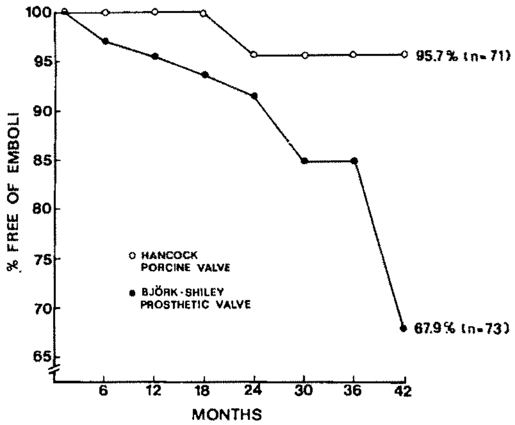
Patient No.	Annulus (mm)	LV-Ao Gradient (mm Hg)	Cardiac Output (L/min)	Aortic Valve Area (cm²)
1	21	10	4.4	1.2
2	21	32	4.5	0.9
3	23	10	4.0	1.2
4	23	30	7.2	1.1
5	25	20	4.4	1.3
6	25	5	3.0	1.2
7	25	5	7.8	2.9

LV = left ventricle; Ao = aorta.

sociated thromboembolic phenomena without the disadvantage of requiring long-term anticoagulation. The Björk-Shiley tilting-disc prosthesis is a hemodynamically effective valve [13], but despite therapeutic levels of anticoagulation, it has a significant associated incidence of thromboembolic phenomena in our experience, including 2 totally thrombosed valves. Based on these data, we recommend no anticoagulants for patients with the porcine valve unless they have chronic atrial fibrillation, but we do use anticoagulation with prosthetic valves.

The durability of the Hancock valve has been satisfactory in our experience during the follow-up period of up to 42 months. We have seen no valve failure from cusp rupture as a result of collagen disruption in the absence of infection. Pipkin and colleagues [12], Hannah and Reis [8], and Zuhdi and co-workers [17] have also documented satisfactory durability for up to five years with the Hancock valve in the aortic position. Zuhdi* reports 12 patients with no dysfunction in Hancock porcine valves at six years. Glutaraldehyde-preserved heterografts were utilized by Carpentier and his associates in 1968 to produce a "bioprosthetic" of porcine xenografts. Long-term follow-up in their series also exceeds six years with a satisfactory durability record [3].

Fig 3. Actuarial curves calculating percentage of patients in each valve group free from emboli at 42 months.



The improved durability of the Hancock xenograft valve over previous xenografts may be related to the method of preparation using stabilized glutaraldehyde. This process apparently is minimally damaging to collagen linkages as measured by shrink temperature determination. Mounting the valve on a flexible stent lessens closure stress as well, since the polypropylene struts may absorb as much as 90% of the pressure load at the tips [13]. Histological appearance and shrink temperature have been unaltered from preimplant specifications in valves recovered up to 56 months after operation [12].

The technique for insertion of this graft is somewhat more demanding than placement of a prosthetic valve. The presence of the struts makes knot tying under the right coronary artery particularly difficult. In an aortic root that is small and not dilated, the struts may impinge on the aortotomy, and closing the aorta may tend to produce secondary outflow obstruction. To overcome this problem, Shumway [16] and

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*Zuhdi N: Personal communication.

Blank and his group [2] have used a prosthetic outflow gusset to enlarge the small annulus and possibly allow the use of a larger valve. In patients who have a small annulus we have generally preferred the Björk-Shiley prosthetic disc valve unless there has been a compelling reason to utilize the nonthrombogenic porcine valve.

In addition to technical problems with a small annulus, the hemodynamic characteristics of the Hancock valve in the small sizes have not been totally satisfactory. Hannah and Reis [8] recently reported data on postoperative gradients in 18 patients with the Hancock aortic valve. Resting gradients from 0 to 38 mm Hg (mean, 16) and exercise gradients from 15 to 125 mm Hg (mean, 70) were documented in the smaller-sized annuli. Morris and co-workers [11] have restudied 20 patients postoperatively and found peak systolic gradients averaging 23 mm Hg at rest and 37 mm Hg during exercise. We measured resting transvalvular gradients in 7 patients and in the 21 mm valve recorded a resting gradient of 32 mm Hg (see Table 3). There is considerable gradient variation in any particular patient, depending upon the cardiac output, systolic ejection time, and effective orifice size, which may vary somewhat from valve to valve. Recent modifications and improvements in the fabrication and mounting of the Hancock porcine valve may allow quantitative improvements in effective orifice area as calculated by planimetry.*

We believe that aortic valve replacement should be individualized according to anatomical restrictions and the patient's overall clinical status. We tend to favor the Björk-Shiley valve in the 19 or 21 mm aortic annulus and the Hancock xenograft for aortic valve replacement in all other annuli. If there is a serious threat of thromboembolism or an absolute contraindication to anticoagulation, a small-sized porcine xenograft valve may be indicated even though a prosthetic valve would have a larger effective orifice. In these cases, the transvalvular gradient should be measured when the patient is stable on cardiopulmonary bypass. If an excessive gradient is found, gusset reconstruction or changing the valve may be indicated.

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Discussion

DR. JOHN H. KENNEDY (Cleveland, OH): I commend Dr. Cohn for his interesting study of aortic valve replacement using chemically modified porcine xenografts.

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*Hancock Laboratories: Personal communication.

As is the case with prosthetic as well as biological replacement for the natural cardiac valve, the quality of the material used for valve replacement is a major factor in late malfunction. The characteristics of the compound biopolymer system depend a great deal not just on collagen cross-linking, referred to by Dr. Cohn, but on the effects that chemical modification may have on the other components of the compound polymer system.

In the case of human material, there is considerable variation in the mechanical behavior of fresh tissue studied at postmortem examination. What effect the glutaraldehyde fixation may have on, for example, stiffening of the valve leaflets later on may also be a factor; we have heard that there are 120 ml gradients in some of these valves. I would like to ask the essayists whether they have any information on the late mechanical properties of the chemically modified valve material.

I should add that I am indebted to Dr. Eric Baer, chairman of my host department at Case Western Reserve University, for some of these data.

DR. ALAIN CARPENTIER (Paris, France): I would like to congratulate Dr. Cohn for his excellent presentation and concentrate my comments on the major problem raised by xenograft valves, which is their durability. Since we introduced the use of glutaraldehyde in preservation of porcine grafts in 1968, we now have an eight-year follow-up. In our first series of patients operated on up to 1972, there were 52 aortic valve replacements. Two methods of glutaraldehyde preservation were used: buffered glutaraldehyde, 0.6%, for the first 11 patients, and oxidation by sodium metaperiodate and buffered glutaraldehyde for the remaining patients. The actuarial curves showed an 80% survival rate and 17% valve failure rate at six years. Most failures, particularly calcification, occurred in valves treated by oxidation and glutaraldehyde; only 1 valve treated by buffered glutaraldehyde alone failed. This latter method is at present used for xenograft preservation by all the manufacturing laboratories.

I would like to point out that most of the failures occurred in valves prepared in our research laboratory before the heterografts became commercially available. It is likely that the incidence of valve failure will be reduced by the use of grafts prepared on a large scale with better manufacturing facilities and superior quality control. Particularly important has been the use of a partially flexible stent (Hancock Laboratories) and, more recently, the development of a fully flexible stent (Edwards Laboratories model). The latter is made of Elgyloil wire covered by Teflon and Dacron cloth. The thickness of the wall has been reduced to decrease the gradient through the valve. The flexibility of the valve improves hemodynamic function and reduces stress at the point of attachment of the cusps. The slight motion does not impair valve competence.

Finally, I would like to emphasize that bioprostheses have a limited durability. Based on actuarial curves of our eight-year experience, we can predict that at the end of ten years the valve failure rate will be 20%. To illustrate this point, we have angiocardiograms showing perfect function of a glutaraldehyde-preserved aortic xenograft valve at eight years. The patient leads a normal life with no medications, particularly no anticoagulants. He represents the longest follow-up of a xenograft valve implanted in a human being.

DR. CARLOS G. DURAN (Santander, Spain): Two years ago we reported to this Society 3 failures of oxidized, glutaraldehyde-preserved, mounted xenografts. Since then we have had 4 further graft failures in a group of 30 patients followed for a maximum of five years, 20 of them for more than four years (a total failure of 23%). I insist that these xenografts had been oxidized when processed.

Obviously, we stopped using this type of graft and moved on to the Hancock valve. We have placed well over 250 such valves so far without any failures. However, we have recently found a small construction problem with the Hancock valve. In 4 instances we have checked the closure of the Hancock valve in the mitral position during operation by filling the left ventricle through the left vent. In all 4 patients three small jets appeared at each commissure, and although I do not think they are hemodynamically significant, they do represent a defective mounting system.

In another patient a more serious problem was found: a jet appeared between the porcine tissue and the frame. She was undergoing triple-valve replacement, and the surgeon decided to carry on with the other valves. She has been recatheterized since then and must be scheduled for reoperation based on a left atrial "v" wave of 40 mm Hg and grade 3/4 angiographic regurgitation.

These are manufacturing problems which I hope will not mar the excellent clinical results with this xenograft.

DR. ROBERT D. PIPKIN (Palo Alto, CA): Dr. Cohn's paper contains several points on which I would like to comment. The reported low incidence of thromboembolism with the Hancock porcine xenograft has been reported by other groups. However, our group, led by Dr. Fogarty, has not had as favorable an experience. From June, 1971, through December, 1975, we have used the Hancock porcine xenograft in the aortic position in 119 patients. There have been 6 suspected embolic episodes, though only 1 has been proved. Five of these were cerebral and 1 was renal. None of these patients was on long-term anticoagulation or in atrial fibrillation at the time of the embolic episode. It is of interest that all occurred within 3 months of the date of implantation. There have been no additional embolic episodes in any of these patients.

We also are concerned about the reported relatively high pressure gradients across some of the smaller Hancock valves. For this reason we take extensive efforts to place as large a valve as possible. In our series of 119 patients we have placed 1 No. 19 valve and 5 No. 21 valves. The average size has been No. 26. None of the patients who received a No. 19 or 21 valve has died. All are doing well with the exception of 1 patient who had been in chronic congestive failure preoperatively and is experiencing it intermittently postoperatively.

We have not restudied any of these patients. We have tried to convince the referring cardiologist to restudy the patient in chronic congestive failure, but he has not yet done so.

Aortic insufficiency, presumably due to perivalvular leaks, occurred in 8 of these patients, all early in the series. None of them has had to undergo reoperation. There have been no valve failures.

Finally, I would like to ask Dr. Cohn one question: How many of these valves became infected? Certainly, up to the present time, the Hancock valve does appear to be resisting infection well.

DR. LEWIS H. BOSHER, JR. (Richmond, VA): Dr. Cohn has presented a very nice paper describing a low incidence of thromboembolic complications. I have a rather uncomfortable feeling about the small-sized Hancock prosthesis, particularly when there is associated left ventricular dysfunction. I had a rather catastrophic experience with one 21 mm Hancock valve. This particular patient, 52 years of age, was admitted for aortic valve replacement because of aortic insufficiency and mild mitral stenosis. She was known to have a significant degree of left ventricular dysfunction. The left atrial wedge pressure rose from 15 to 45 mm Hg with one minute of exercise. The cardiac index was 1.9.

She was operated upon uneventfully and discharged about 10 days later, although still taking digoxin and 80 mg of Lasix a day and experiencing atrial fibrillation. She was readmitted one week later in progressive congestive failure, for which she was treated, but she died fairly promptly. We had been lulled into a sense of security about the low thrombotic potential of the Hancock valve and missed a golden opportunity to get the valve out.

At postmortem examination there was a residual 7 mm orifice at the apex of the prosthesis. The sinuses were almost completely bridged by clot and fibrin with a trailing thrombus extending into the aorta. There was no evidence of infection. In the smaller-sized prostheses, the posts are relatively large and the sinuses are proportionately small. This geometry may facilitate the buildup of fibrin.

As a result of this experience we have stopped using Hancock aortic prostheses in the small sizes and will use some other valve if we have to place a Hancock smaller than size 25.

DR. COHN: I thank all the discussants for their informative comments and would like to make a couple of general points related to their questions.

Durability, of course, still is a very important problem. Some mitral valve porcine xenografts stabilized by the Hancock glutaraldehyde process have been recovered 56 months after implantation. Shrink temperatures, which are a very good estimate of the collagen cross-linkages, were apparently exactly the same as in the preimplantation specimens.

We have had 2 patients die from infection. Endocarditis on the valve developed in a man who had documented endocarditis but for some reason did not come to the hospital for treatment until quite late. The other infection was not on the valve but on the suture line of an aortotomy, which resulted in a false aneurysm. Interestingly, we have had 1 patient with xenograft endocarditis recover from the infection completely after antibiotic treatment.

We have no data to support whether it is more or less susceptible to infection, but we have no hesitation about placing it in patients with acute endocarditis if the annulus size is correct. No patient in our series who underwent porcine valve replacement for endocarditis has subsequently developed endocarditis on the new valve.

Surgical Treatment of Large Ventricular Septal Defect with Pulmonary Hypertension in the First 24 Months of Life

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and Ichiki Kanoh, M.D.

ABSTRACT **A total of 74 patients under 24 months of age with large ventricular septal defects (VSD) and pulmonary hypertension were subjected to surgical treatment from 1969 through 1975. Emergency pulmonary artery (PA) banding was performed in 13 patients during the first year of life with 1 death from postoperative respiratory failure. Primary closure of the VSD was performed in 61 patients using simple hypothermia and short-term coronary perfusion, with an operative mortality of 1.6%. There were no late deaths or neurological disturbances. Normal hemodynamic data were obtained in all 7 patients who underwent postoperative cardiac catheterization from one month to five years after the primary correction.**

It is concluded that primary closure of a VSD in infancy is reasonable and that PA banding is indicated only for those patients less than 6 months old with a complicated defect or in an emergency situation.

Since 1961 we have been performing primary closure of ventricular septal defects (VSD) during infancy [13, 14, 23], and since 1969 we have employed pulmonary artery (PA) banding in emergency situations for patients less than 1 year old and have done primary closure of VSDs on an elective basis. This paper describes the results of surgical treatment since 1969 in 74 consecutive patients, all under 2 years of age, and discusses the indications for surgical treatment of a large VSD in infancy.

Clinical Material

Between January, 1969, and June, 1975, 74 patients under 2 years of age were referred to our service for surgical treatment of a VSD with pulmonary hypertension. Indications for surgical treatment were: (1) intractable congestive heart failure despite medical treatment; (2) poor weight gain or frequent dyspneic attacks; and (3) progressive obstructive pulmonary vascular disease. The age distribution is shown in Figure 1 and body weights are listed in Table 1.

The preoperative hemodynamic determinations are shown in Table 2. There was no significant difference in hemodynamic data between the patients undergoing PA banding and those having primary repair. The pulmonary/systemic resistance ratio (R_p/R_s) was significantly lower in the patients under 6 months of age than in those in their second year of life ($0.001 < p < 0.01$). The electrocardiogram showed left ventricular hypertrophy in 3 patients, right ventricular hypertrophy in 15 patients, and hypertrophy of both chambers in 56 patients. The cardiothoracic ratio ranged from 52 to 72% with a mean of 60%.

Primary repair was performed electively in 61 patients; the remaining 13 underwent emergency PA banding for repeated congestive heart failure, pulmonary edema, and atelectasis or dyspneic attacks.

Methods

Hypothermia

Atropine sulfate (0.02 mg per kilogram of body weight) was administered intramuscularly as premedication. After anesthesia had been induced with halothane, triflupromazine (1 mg/kg) and low-molecular-weight dextran (10 ml/kg) were given intravenously. The brachial

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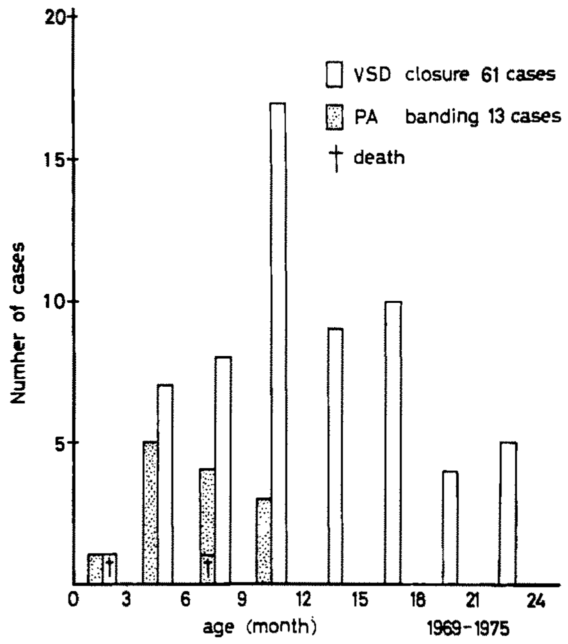

Fig 1. Age distribution of the 74 patients undergoing closure of a ventricular septal defect or pulmonary artery banding.

Table 1. Distribution of Body Weight

Age (mo)	Procedure	No. of Patients	Body Weight (kg) Range	Mean
2–5	PA banding	6	3.8–5.0	4.7
	VSD closure	8	4.5–6.2	5.4
6–11	PA banding	7	5.0–6.2	5.7
	VSD closure	24	3.8–8.3	6.1
12–23	VSD closure	29	5.4–12.2	7.7
Total		74		6.5

PA = pulmonary artery; VSD = ventricular septal defect.

or femoral arterial pressure was continuously monitored. Under deep ether anesthesia the patient was cooled in an ice-water bath at a rate of 2°C every 5 minutes. The anesthesiologist provided assisted ventilation. When the patient reached 28°C, he was placed on a cooling blanket on the operating table and a median sternotomy incision was made. When the pharyngeal temperature had fallen to about 25°C, the pericardium was opened. A coronary perfusion cannula was placed in the ascending aorta, with heparin (1 mg/kg) administered intravenously before cannulation.

The superior and inferior venae cavae were snared, and when the heart had emptied, the ascending aorta and pulmonary arteries were also occluded. Normal sinus rhythm was usually maintained with an arterial pressure of 45 to 55 mm Hg systolic until inflow occlusion began. Cardiac massage has not been necessary.

VSD Closure

The septal defect was closed with a Teflon patch through a right ventriculotomy under total circulatory arrest of 25 to 30 minutes. Just before the last stitch was tied the aortic valve was made incompetent by inserting an instrument through the VSD, and coronary perfusion was started using a roller pump. The line pressure (50 to 100 mm Hg) and flow rate (7 to 10 ml/kg/min) were continuously monitored. While coronary venous blood was being sucked through the right ventriculotomy, the ventriculotomy was closed and the acid-base balance was corrected. After 2 to 3 minutes of coronary perfusion the heart ordinarily started to beat vigorously, although electrical defibrillation

Table 2. Preoperative Hemodynamic Data in the 74 Patients

Age (mo)	No. of Patients	P_p/P_s	R_p/R_s	Q_p/Q_s
1–5	14	0.65 ± 0.18	0.15 ± 0.05[a]	3.8 ± 2.0
6–11	31	0.71 ± 0.18	0.25 ± 0.13	3.0 ± 1.5
12–23	29	0.76 ± 0.17	0.31 ± 0.17[a]	2.5 ± 0.9

[a] $0.001 < p < 0.01$; mean ± SD.

P_p/P_s = pulmonary/systemic peak systolic pressure ratio; R_p/R_s = pulmonary/systemic resistance ratio; Q_p/Q_s = pulmonary/systemic flow ratio.

was occasionally required. Sodium bicarbonate solution (10 to 20 ml) was given intravenously.

Once the heart was contracting vigorously, inflow and outflow occlusion were discontinued. The heart was usually able to maintain an acceptable blood pressure of 40 to 50 mm Hg systolic. If bradycardia occurred, epicardial pacing was employed for a short period. An intraventricular injection of noradrenaline (0.3 mg) was also effective in increasing heart rate and blood pressure.

Rewarming

In order to induce central warming, the heart was irrigated with warm saline and the blanket was filled with warm fluid for surface heating. The wound was closed at a pharyngeal temperature of 28°C, and the patient was placed in a hot-water bath. The changes in temperature, heart rate, blood pressure, and blood gas values throughout the procedure are shown in Figure 2. Cardiac massage has not been necessary with this method of cardiac resuscitation, and the patient awakens in the recovery room.

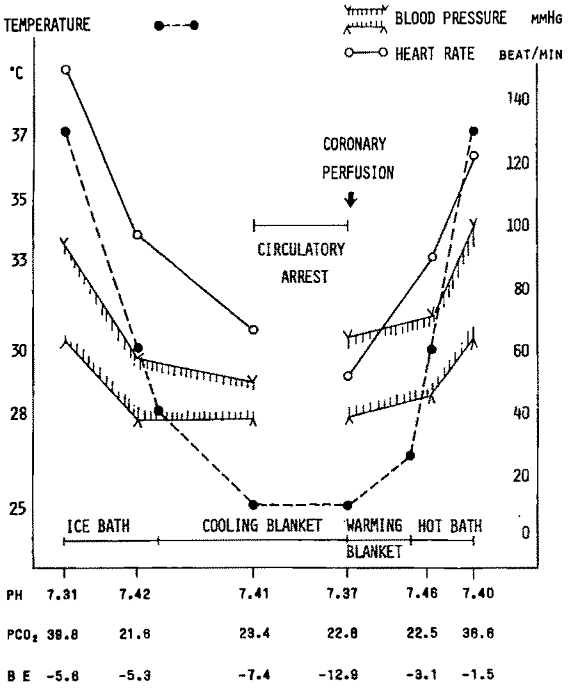

Fig 2. Changes in temperature, heart rate, blood pressure, and blood gas values during simple hypothermia and coronary perfusion. Data indicate the average after temperature correction. (BE = base excess.)

Pulmonary Artery Banding

Using Teflon tape 6 to 9 mm wide, the pulmonary artery was banded to the point that pulmonary artery systolic pressure was reduced to below 50% of systemic pressure. Usually this meant that the pulmonary artery was reduced to one-third to half of the original diameter, and the systemic pressure was raised 10 to 20 mm Hg. The tape was anchored to the pulmonary arterial wall to prevent migration.

Results

VSD Closure

Among the 61 patients with VSD, patent ductus arteriosus coexisted in 4 and an atrial septal defect in 3. A 2-month-old baby died during operation from hyperpotassemia (K^+ of 11 mEq/L) of the perfusing blood due to hemolysis, which was caused by an antibody incompatibility of 2 different donors. This represented an operative mortality of 1.6%. The remaining 60 patients survived operation and were discharged from the hospital in good condition.

The VSD was located in the supracristal portion of the ventricle in 8 patients, in the membranous portion in 52, and in the inflow portion in 1. The VSD was more than 10 mm in diameter in most instances, necessitating patch closure in all but 2 patients. The endotracheal tube was removed within 6 hours in most cases. Intensive respiratory care for more than 24 hours was required in only 4 patients (6.6%).

Postoperative complications occurred in 5 patients who were operated on in their first year of life: a tracheostomy was required in 2 patients; complete atrioventricular block occurred in 2 others and necessitated insertion of a permanent pacemaker; and a residual shunt was found in 2 patients, 1 of whom was reoperated upon the next day (this was 1 of the 2 who had developed complete atrioventricular block).

The mean cardiothoracic ratio one year after operation was 55%, and body weight had reached the normal range in most cases. All survivors are asymptomatic at this time except for 1 patient who was mentally and physically retarded due to preoperative cerebral palsy. Neurological studies, consisting of electroencephalography and determination of developmental quotient, were performed in the 7 most recently treated patients prior to and one month after hypothermic anesthesia to evaluate possible brain damage. The studies showed no abnormalities.

The results of postoperative catheterization one month to five years (average, thirty-four months) after primary correction are compared with the preoperative data in Figure 3. No patient developed progressive obstructive pulmonary vascular disease.

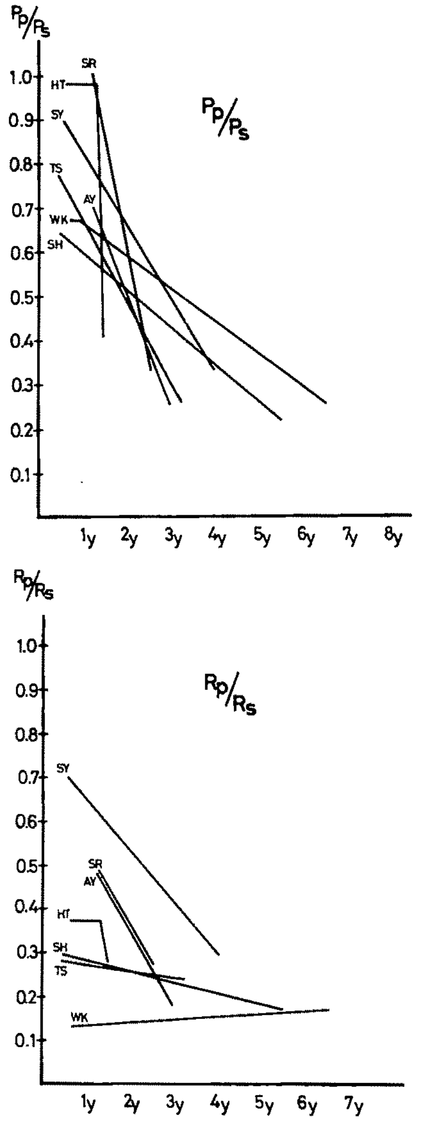

Fig 3. Hemodynamic changes in 7 patients who underwent repeat cardiac catheterization following primary closure of VSD. (A) Pulmonary/systemic peak systolic pressure ratio. (B) Pulmonary/systemic resistance ratio.

PA Banding

Among the 13 patients with pulmonary hypertension, patent ductus arteriosus coexisted in 4 and atrial septal defect in 3. Intensive respiratory care for seven days to three months was required in 4 babies, 1 of whom—an 8-month-old boy—died from respiratory failure on the twentieth postoperative day, an operative mortality of 7.7%. Another patient developed an aneurysm of the pulmonary artery secondary to septicemia. This patient was saved by secondary closure of the VSD and aneurysmectomy six months after the PA banding when the inflammation had subsided. The tape was found suspended in the aneurysm at the time of the second operation. The remaining 11 patients showed remarkable improvement.

Elective secondary correction was performed in 5 of these 11 patients two to four years after the PA banding without any operative deaths. Their body weights were all within normal range at the time of the staged correction. Cardiac catheterization data before the first and second operations are compared in Table 3. Obstructive pulmonary vascular disease was effectively prevented. Three of the 5 patients required patch arterioplasty of the pulmonary artery. Postoperative management was relatively easy in all cases.

Comment

The primary indications for surgical treatment of a large VSD in the first year of life are life-threatening, intractable heart failure or respiratory insufficiency. Sixteen percent of the patients with a large VSD ($Q_p/Q_s > 2.0$) are in this

Table 3. Hemodynamic Data in 5 Patients Undergoing Staged Correction[a]

Determination	Before PA Banding	Before Correction
P_p/P_s	0.45–0.74 (0.61)	0.15–0.57 (0.34)
R_p/R_s	0.06–0.53 (0.22)	0.11–0.39 (0.26)
Q_p/Q_s	2.8 –6.0 (4.2)	0.83–1.23 (1.1)

[a] Age at PA banding: 1 to 9 mo (average, 5.8 mo); age at secondary correction: 2 yr 8 mo to 4 yr 4 mo (average, 3 yr 7 mo).

Symbols same as in Table 2.

group [4]. The purpose of surgical treatment in the second year of life is to prevent obstructive pulmonary vascular disease. Friedli and colleagues [8] demonstrated that closure of the VSD after 2 years of age cannot always prevent progressive obstructive pulmonary vascular disease in those patients in whom the R_p/R_s is greater than 0.33.

Reports from the Hospital for Sick Children, Toronto [8], and the Mayo Clinic [6] and our own results support the concept that progressive obstructive pulmonary vascular disease can be interrupted by closing the VSD before 2 years of age. The risk from closure of VSD in the second year of life is quite low. We have had no operative deaths or persistent atrioventricular block in 29 consecutive patients in this series. Therefore, progression of the Eisenmenger syndrome can easily be halted by cardiac catheterization followed by surgical closure of the VSD in the second year of life. Furthermore, by evaluating asymptomatic patients who had been operated on for VSD with pulmonary hypertension three to fifteen years previously, Maron and colleagues [15] demonstrated that the magnitude of the postoperative abnormality in cardiac output response to exercise is directly related to age at the time of operation and that there is a positive correlation between pulmonary arterial pressure during intense exercise and the age at operation. This information appears to justify early correction if the procedure is safe.

Since Muller and Dammann [19] described PA banding in 1952, the excellent palliative effect of the procedure has been documented. Marked improvement in clinical status was also obtained in all our patients except for the one who developed an infection. However, the final results, including operative mortality and morbidity, should be compared between staged correction and primary repair. The mortality of PA banding has been 5 to 25% and that of secondary repair, 12 to 28% [11]. The best result reported has been an overall mortality of 15% [9]. Besides the direct mortality, numerous complications from PA banding have been reported in the literature, such as progression of subaortic [7] or subpulmonic stenosis [11], paradoxical embolism [15], thickening of the pulmonic valve [11], stenosis or obstruction of the right pulmonary artery by the band [11], persistent pulmonary hypertension [10], calcification or rupture of the pulmonary artery [10], difficulty of debanding, increased right ventricular load due to spontaneous closure of the VSD causing sudden death [21], and restenosis of the pulmonary artery after secondary repair [5].

On the other hand, since the technique for primary correction of VSD in infancy under hypothermia was developed by us in 1963 [14], Mohri and co-workers in 1966 [17], and Hikasa and associates in 1967 [12], the procedure has gained widespread acceptance throughout the world. The operative mortality for primary closure in the first year of life has become acceptable. However, if we focus on patients under 6 months of age, the operative mortality from primary closure of VSD varies from 0 to 66%, as shown in Table 4 [1, 3, 16, 18, 20, 22]. Our mor-

Table 4. Results of Primary Repair of a Large VSD before 6 Months of Age

Institution	No. of Patients	Mortality (%)	Method
Green Lane Hospital [1]	8	0	Surface & core cooling
Boston Children's Hospital [3]	9	33	Surface & core cooling
University of Texas, Dallas [22]	1	0	Normothermia
Washington University [20]	9	33	Surface cooling
Tokyo Women's Medical College [18]	3	66	Surface & core cooling
Osaka University [16]	3	0	Surface & core cooling
Tohoku University	8	13	Surface cooling & coronary perfusion

tality was 13% in this series. The number of patients under 6 months of age undergoing primary closure of a VSD is too small for comparison with the results of PA banding. The results of early repair of a VSD associated with coarctation or of multiple VSDs (so-called Swiss cheese ventricular septum) have been poor [2, 3, 20, 21]. Pulmonary artery banding should be considered in these situations as well as for other diagnoses. Considering the possibility of spontaneous closure of the VSD, remission of symptoms after 12 months of age, and higher operative mortality and morbidity in the first year of life, it is preferable to close the VSD after 12 months of age, when the operative risk is low. However, primary closure of the VSD should be selected even in the first year of life for patients with intractable congestive heart failure. Banding is indicated only for patients under 6 months of age with a complicated defect or in an emergency situation.

We are currently using a combination of surface and core cooling for repair of more complicated congenital heart defects such as transposition of the great arteries, complete atrioventricular canal, and tetralogy of Fallot, but profound hypothermia is not always necessary for closure of an uncomplicated VSD. Simple hypothermia with short-term coronary perfusion is a rather safe method of resuscitation that does not affect homeostasis. Cardiac massage is not necessary at all. Postoperative respiratory management was quite easy in most of our patients. Neurological examination by means of electroencephalograms and developmental quotient assessment confirmed that circulatory arrest for 30 minutes at 25°C was harmless to the brain.

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The Blalock-Taussig Operation: The Procedure of Choice in the Hypoxic Infant with Tetralogy of Fallot

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ABSTRACT **From 1971 to 1975, 17 consecutive patients aged 1 day to 4 years underwent Blalock-Taussig shunts for severe tetralogy of Fallot. Three infants were under 6 weeks of age and 7 (41%) under 1 year. There were no hospital deaths. Modification of the shunt technique adapts it to any size infant. The subclavian artery is divided at its major branches and the end spatulated to enlarge it. The artery is occluded while the shunt is constructed.**

No intraoperative complications were encountered; all patients have a shunt murmur with no early or late closure. No child has had heart failure or hypoxic spells. Flows measured at operation equaled one-quarter to one-half of the child's normal cardiac output. Ligation of the shunt at subsequent repair is uncomplicated. One child died three years later at correction from causes unrelated to the shunt.

With appropriate modifications in technique, the Blalock-Taussig shunt is the operation of choice, at any age, for palliation of severe tetralogy of Fallot.

Recent advances in techniques for the correction of tetralogy of Fallot in infancy [1–8] have not yet eliminated the need for creation of a systemic–pulmonary artery shunt as an emergency lifesaving procedure in the acutely ill, hypoxic infant. Until recently, the Blalock-Taussig shunt [3] has been avoided in infants under 1 year old for technical reasons; the Waterston shunt (ascending aorta–right pulmonary artery anastomosis [12, 13]) has been preferred. With a modification in technique, and with the availability of microvascular methods, it is now possible to perform the Blalock-Taussig shunt even in very young infants. This report summarizes our experience with the Blalock-Taussig shunt in 17 consecutive children with severe tetralogy of Fallot.

Clinical Material and Technique

In the four-year period from July, 1971, to July, 1975, 17 consecutive children, 11 boys and 6 girls aged 1 day to 4 years, underwent a Blalock-Taussig shunt for severe tetralogy of Fallot. Seven infants (41%) were 1 day to 12 months old and weighed between 3.1 and 9.6 kg (3 infants were 1 day to 5 months old and 4 were 7 to 12 months old). The indications for the procedure were cyanosis, irritability, and progressive diminution of exercise tolerance in all the children, with hypoxic episodes in 3.

A standard posterolateral thoracotomy incision was used, with entry into the chest through the fourth intercostal space. The side chosen for operation was the one where the subclavian artery originates from the innominate artery rather than from the aorta (see the Figure); this gives the subclavian artery a gentle and uniform curve and minimizes the chance of kinking.

The subclavian artery was dissected up to its distal branches, including the vertebral artery. These branches were ligated at the thoracic inlet, and the subclavian artery was divided just ahead of its branching into the various vessels. The vessel was clamped proximally and delivered under the recurrent laryngeal nerve. Dissection around the innominate artery gave further length and mobility to the subclavian vessel. The end of the divided subclavian artery was then spatulated (Figure), and heparin in a single dose of 1 to 2 mg per kilogram of body weight was given intravenously before the subclavian artery was occluded. The anastomosis to the right or left main pulmonary artery was per-

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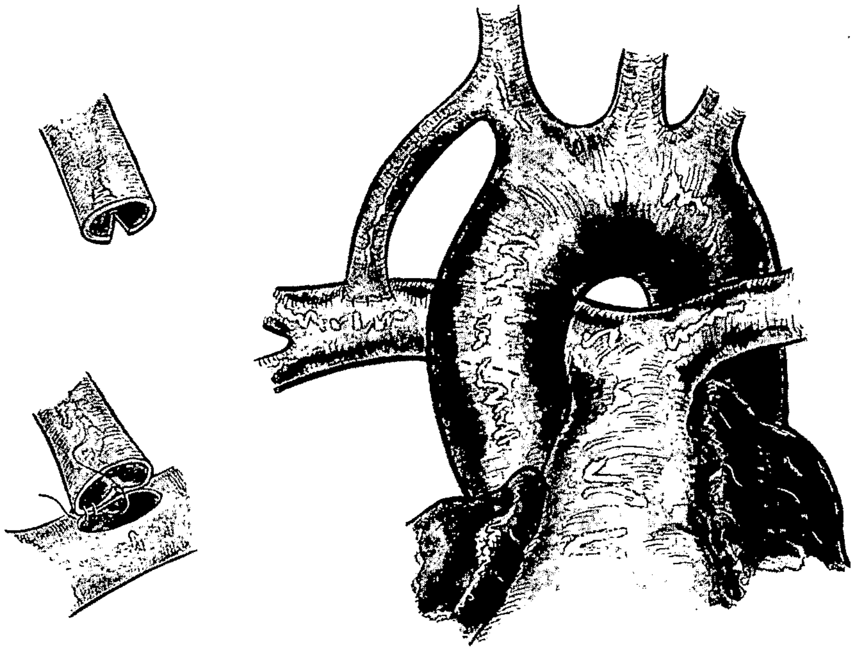

The end of the subclavian artery is spatulated prior to its anastomosis to the right pulmonary artery, and the continuous posterior suture is shown.

formed using a continuous 7-0 polypropylene suture. A continuous suture was used for the posterior wall of the anastomosis and interrupted sutures for the anterior wall. Magnification was utilized while operating on the smaller sized vessels whenever necessary.

There were no intraoperative complications. All patients had a shunt murmur immediately after operation. As an additional objective indicator of the adequacy and patency of the anastomoses, we measured flows through them at the time of operation using a Statham flowmeter. Flows ranged from 256 ml per square meter of body surface area (BSA) to 1,480 ml/m^2, with an average of 557 ml/m^2. These flows equaled from one-quarter to one-half of the child's normal cardiac output and provided the necessary blood flow to the lungs [4].

Results

There were no early or late deaths from the shunt procedure. The follow-up period is 332 patient-months with an average of 20.8. All children had a shunt murmur at the time of postoperative examination. There were no instances of postoperative congestive heart failure. All children have demonstrated increased pulmonary blood flow to both lung fields on follow-up chest roentgenograms. One child, who had a postoperative shunt flow of 1,071 ml/m^2, had mild cardiomegaly on chest roentgenogram and left ventricular hypertrophy by electrocardiographic criteria.

Seven children have undergone correction of tetralogy of Fallot since their shunt procedure at an interval ranging from 21 to 41 months. In all these children the shunt was found to be patent at the time of definitive repair and was simple to take down, thereby not increasing the risk of total correction.

Comment

Until recently, the Waterston shunt [12, 13] and the Blalock-Taussig anastomosis [3] were the two most frequent operations used for palliation of severe tetralogy of Fallot. Kaplan and associates [5] reported that a second palliative operation was required in 45% of their patients when the Blalock-Taussig shunt was done in the first year of life. This has not been our experience nor that of Wood and colleagues [14], who recently reported a series of 18 patients in whom the shunt was performed. The Potts anastomosis has been the least preferable shunt in these patients because of the associated problems of congestive heart failure and the difficulties encountered during later correction [10].

In addition to the ease of taking the shunt down at the time of total repair, the most obvious advantage of the Blalock-Taussig shunt is the fact that postoperative congestive heart failure is rarely encountered with it, as the diameter of the subclavian artery is the ideal size conduit for the shunt. This is proved by the blood flow measurements that we obtained at operation. Follow-up examinations up to four years have demonstrated that these operative flows are more than adequate in providing optimum palliation without producing either pulmonary hypertension or congestive heart failure. The Waterston procedure is often followed by the development of congestive heart failure [2, 9] and pulmonary hypertension; these problems are also common with the Potts anastomosis [10]. Pulmonary hypertension after a Blalock-Taussig shunt, however, is extremely rare [5].

It is now well established that an improperly performed Waterston shunt, in addition to the previously mentioned problems, can often cause kinking and distortion of the right pulmonary artery with shunting of the entire blood flow to the right lung [9]. Tay and associates [9] recently reported a mortality with the Waterston shunt of 40% in infants under 1 week of age and 38% in those under 1 month. The long-term mortality in infants with the Waterston shunt was 53%. At the time of correction, the mortality in these infants is as high as 40% due to the problems encountered in taking down the shunt. In our present series only 1 child who underwent total repair (three and one-half years after the Blalock-Taussig shunt) died postoperatively. The cause of death was unrelated to the shunt but was secondary to low cardiac output.

In our limited series of patients we have shown that the Blalock-Taussig shunt can be performed in even the smallest of infants with low mortality and morbidity and excellent long-term patency. The advantages of this shunt over any other are: (1) a lower incidence of postoperative congestive heart failure and pulmonary hypertension; (2) easy control of the shunt and lack of complications at the time of subsequent correction; and (3) superb palliation up to the time of total repair, with blood flows of up to one-quarter to one-half of the child's cardiac output through the shunt and without any of the undesirable effects of excessive pulmonary blood flow.

We conclude that with appropriate modifications in technique, the Blalock-Taussig shunt is the operation of choice, at any age, for palliation of severe tetralogy of Fallot.

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Discussion

DR. EOIN ABERDEEN (New York, NY): I support the theory that the Blalock-Taussig shunt can be done effectively in the first days and weeks of life. My experience has been with 23 patients in the last five years, most under 1 year of age and 5 in the first week of life. I have been surprised at how effectively the shunts have performed and how well the patients have survived in what now amounts to a five-year follow-up for the oldest.

A technical point I would add is that I believe in dissecting the common carotid artery on the right side. I think there is no point in attempting the operation very early, in the first week of life, except using the innominate artery side. The common carotid should be dissected right up into the neck (it comes out almost like spaghetti), and since the innominate artery junction lies close to the pulmonary artery, a good shunt can be constructed right at the first branch of the subclavian artery. I think that using fine sutures (I prefer 7-0 Prolene) is an important aspect of the procedure. The survivors do surprisingly well with all shunts remaining effectively patent, and I support Dr. Chopra's view on the success of this procedure in very young infants.

I would also point out that Mr. Waterston has always considered the Blalock-Taussig the shunt of choice if it will work, and I think we have shown that it can be effective even in the smallest babies.

DR. EDUARDO ARCINIEGAS (Detroit, MI): At Children's Hospital in Detroit we defer correction of tetralogy of Fallot until the child is 4 to 5 years old. During the past four years complete repair has been done in 110 patients with 5 deaths. Until recently we had generally reserved the Blalock anastomosis for children over 1 year of age and did Waterston shunts in those below 1 year. The Waterston group comprises 37 patients with 1 death and 3 early reoperations for oversized shunts. The group with Blalock shunts totals 69 patients, of whom 45 had tetralogy of Fallot.

During the past two years Blalock shunts have been done in 28 patients under 1 year, not only with tetralogy but with other cyanotic lesions as well. Fourteen patients were operated on within the first 3 months of life, 7 at less than 1 week old. There were no deaths in this group, and all had a good shunt murmur postoperatively. All shunts have remained open at late follow-up.

We share Dr. Chopra's belief that the Blalock-Taussig shunt, if properly done, is the procedure of choice even in the tiniest infants. We use the subclavian artery coming off the innominate to avoid kinking, mobilize the carotid artery extensively to avoid tension, and divide the subclavian artery at the origin of the first branch to obtain the largest possible anastomosis, which is then made with 7-0 Prolene sutures. The use of either heparin or vasopressors has not been necessary.

DR. JAY L. ANKENEY (Cleveland, OH): I wish to congratulate Dr. Chopra and his associates for this excellent presentation and their outstanding results. I support completely their conclusion that the Blalock-Taussig shunt is the palliative treatment of choice in tetralogy of Fallot.

Our experience is quite similar to that of the authors, in that the operative mortality for creating a subclavian-pulmonary artery shunt is very low. In our experience over many years we have lost 2 patients; both were under 6 months of age and died in 1957 or 1958, before the era of coronary artery bypass surgery. We have now done Blalock-Taussig shunts in 10 patients under the age of 1 year with satisfactory results.

Of great importance is the fact that subsequent repair may be carried out safely. We have had only 2 deaths in the 26 patients who have undergone repair following Blalock-Taussig shunts, and neither death was related to the shunt being present. In contrast, the operative mortality initially is much higher in patients undergoing creation of an aortopulmonary shunt, and this type of anastomosis—at least in our hands—contributes to the mortality at subsequent correction. Of our 4 operative deaths during later repair, 2 were due to pulmonary vascular resistance that had developed as a result of the shunt's being too large, and the other 2 were due to my inability to handle the obstructive right pulmonary artery correctly.

This beautiful demonstration by the authors that the hypoxic infant with tetralogy can be treated effectively with a palliative Blalock-Taussig shunt raises the question of whether or not repair of tetralogy of Fallot should be done during the first year of life. This question is especially pertinent since we do not know the fate of the reconstructed right ventricular outflow tract, which is almost always needed for complete repair of tetralogy of Fallot in infants. On the other hand, we know that correction of tetralogy performed in older children is tolerated well into childhood.

In closing, I would like to ask the authors at what age they plan to carry out the correction.

DR. CHOPRA: Dr. Aberdeen, thank you for your remarks. We do indeed free up the common carotid artery—I just did not mention it. Another minor point I failed to mention is that, as the late Dr. Gross suggested, freeing the inferior pulmonary ligament to elevate the hilum will further reduce tension at the site of the anastomosis.

Dr. Arciniegas, I congratulate you on your excellent series. We do agree on this being the procedure of choice in the hypoxic infant. I might reemphasize that the results reported here were only those related to Blalock-Taussig shunts done for infants with severe tetralogy of Fallot.

Dr. Ankeney, thank you very much for your kind remarks. We also have had problems with the Waterston shunt at the time of total repair, and we do our corrections for tetralogy when the children have reached about 4 years of age.

Use of the Doubly Tapered Graft for the Creation of a Systemic–Pulmonary Arterial Shunt

Nina S. Braunwald, M.D., and Aldo R. Castaneda, M.D.

ABSTRACT **It is now possible to construct vascular grafts of expanded polytetrafluoroethylene having complex configurations. In this series of experiments a double tapered graft was used to create a bypass shunt between the aorta and the pulmonary artery in rhesus monkeys and between the aorta and the iliac artery in dogs. When the synthetic material was placed under a slight degree of tension, a high degree of patency was achieved in animals killed three to six months following implantation.**

The use of this approach in neonates with cyanotic congenital heart disease necessitating the creation of systemic–pulmonary artery shunts is suggested as a new method to achieve a controlled lumen size and an increased patency rate, while simultaneously decreasing the incidence of congestive heart failure or of late stricture of the pulmonary artery.

The concept of improving systemic oxygenation in patients with cyanotic congenital heart disease and diminished pulmonary blood flow and pressure by creating a shunt between the subclavian and pulmonary artery—the Blalock-Taussig shunt—was introduced clinically in 1945 [1]. It was found to be particularly effective in the treatment of patients over the age of 6 months. In younger infants, particularly those operated upon during the first few weeks of life, thrombosis of the shunt is not uncommon. This complication is related in part to the small size of the anastomosed vessels. In an effort to circumvent this problem, Waterston [8] in 1962 created a direct shunt between the ascending aorta and the right pulmonary artery. Occasionally this shunt produces some degree of tension on the very small pulmonary artery, which results in late stenosis or occlusion of the pulmonary artery.

Recent advances in the fabrication of synthetic materials suggested that a doubly tapered graft made of expanded microporous polytetrafluoroethylene (PTFE)* might provide the basis for an improved method of creating a communication between the aorta and pulmonary artery. This graft has the advantage of allowing more precise control of the amount of blood flow through the center of the shunt while at the same time providing a tube of larger diameter at each end for performance of the anastomosis. The experimental study using this graft is described in this report.

Materials and Methods

Doubly tapered grafts of expanded PTFE were specially fabricated for this study (Fig 1). One version consisted of a graft with a central diameter of 3 mm, widening to 5 mm at each end (referred to as a 5-3-5 graft); in the other the diameter of the central portion was 4 mm, widening out to 6 mm at each end (referred to as a 6-4-6 graft). Straight grafts 4 mm in diameter were also implanted. The pore size of the material ranged between 30 and 100μ and was determined by the length of the fibrils, a factor controlled during the fabrication process.

Group A

The tapered grafts were anastomosed end-to-side between the left pulmonary artery and descending aorta in 10 rhesus monkeys weighing between 3.6 and 9 kg. These were considered the experimental group. The vessels were exposed through a left thoracotomy. The pulmonary artery and aorta were temporarily occluded with vascular clamps. The anastomoses were carried out using microsurgical techniques with optical glasses having a magnification of 3×. Inter-

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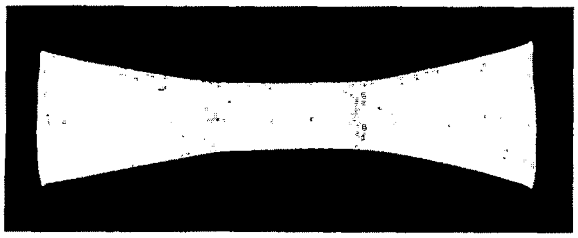


Fig 1. A doubly tapered polytetrafluoroethylene graft with an internal diameter of 3 mm centrally, widening out to 5 mm at each end (5-3-5 graft).

rupted sutures of 6-0 Prolene were placed at each end of the vessel, and the anastomoses were completed with a continuous over-and-over stitch. The grafts were flushed with 2 ml of heparinized saline before releasing the clamps. The incisions were closed in layers, and ampicillin, 0.5 gm, was administered intramuscularly twice daily for five days postoperatively. Straight grafts 4 mm in internal diameter were inserted between the descending aorta and left pulmonary artery in 5 monkeys that served as controls.

In the first 5 experimental monkeys, in which a tapered graft was inserted between the aorta and pulmonary artery, and in the 5 control monkeys, in which a straight 4 mm graft was used in the same location, the graft was positioned with some degree of slack so that it tended to assume an arc configuration following expansion of the lung. In the other 5 experimental primates, the tapered graft was deliberately positioned under some degree of tension by selecting a shorter length of graft to suture between the aorta and pulmonary artery than was used in the first 5 monkeys.

Group B

Doubly tapered 5-3-5 grafts connected the side of the aorta with the side of the right common iliac artery in 5 mongrel dogs weighing between 6.75 and 13.5 kg. The vessels were exposed through a rectus-splitting incision. The anastomoses were carried out with a continuous suture of 6-0 Prolene. The iliac artery was doubly ligated with suture ligatures of 3-0 Tevdek and was divided at the completion of graft insertion in order to put some degree of tension on the graft. The incision was closed in layers, and ampicillin was administered for five days as in Group A. The animals were examined at monthly intervals, and the presence and quality of the femoral pulse on the operated side were noted.

Groups A and B

The animals were electively sacrificed at intervals from three to six months postoperatively. The internal diameters of each graft both in its central portion and at the anastomotic sites were determined by the insertion of vascular probes marked in millimeters and positioned along the length of the graft. Gross and microscopical examination of all specimens was carried out on a routine basis.

Results

All animals were healthy at the time of elective sacrifice three to six months postoperatively. No excessive bleeding through the grafts was encountered in any instance.

Group A (Pulmonary Artery–Descending Thoracic Aorta Grafts in Rhesus Monkeys)

Two of the 5 tapered grafts which were positioned with some degree of slack (Table 1) and 2 of the 5 straight 4 mm grafts (Table 2) placed end-to-side between the left pulmonary artery and the descending aorta were kinked and thrombosed at the time the animals were killed three months postoperatively. All 5 of the tapered grafts in which shorter lengths were selected to complete the shunt, thereby producing slight tension along the length of the graft, were patent when examined three to six months postoperatively (Table 3).

Gross pathological examination of the patent grafts in both the straight and tapered configurations revealed that they were covered with a thin, shiny layer of neointima throughout their length which also extended over the suture lines (Fig 2). Measurement of the internal diameter of the grafts at the time of sacrifice three to six months postoperatively revealed a 1 mm decrease in diameter at the anastomotic site which appeared to be caused by the creation of the suture line together with the overlying neointimal layer. In the case of the 5-3-5 mm tapered grafts, it was still possible to pass a 3 mm probe through the central portion of the graft. The

Table 1. Results following Insertion of a Doubly Tapered Graft from the Left Pulmonary Artery to the Descending Aorta in Rhesus Monkeys

Monkey	Configuration	Duration of Implantation	Findings
F	6-4-6[a]	3 mo	Excessive slack; kinked, thrombosed
G	6-4-6	3 mo	Excessive slack; patent
H	5-3-5	3 mo	Excessive slack; patent
I	5-3-5	3 mo	Excessive slack; kinked, thrombosed
J	5-3-5	3 mo	Excessive slack; patent

[a] End-central-end graft internal diameters in millimeters.

Table 2. Results following Insertion of a Straight Graft from the Left Pulmonary Artery to the Descending Aorta in Rhesus Monkeys (Control Animals)

Monkey	Configuration	Duration of Implantation	Findings
A	Straight (4 mm[a])	3 mo	Excess slack; kinked, thrombosed
B	Straight (4 mm)	3 mo	Patent
C	Straight (4 mm)	3 mo	Excess slack; kinked, thrombosed
D	Straight (4 mm)	3 mo	Patent
E	Straight (4 mm)	3 mo	Patent

[a] Internal diameter.

Table 3. Results following Insertion of a Doubly Tapered Graft under Tension from the Left Pulmonary Artery to the Descending Aorta in Rhesus Monkeys

Monkey	Configuration	Duration of Implantation	Findings
L	6-4-6[a]	3 mo	Patent
M	5-3-5	3 mo	Patent
N	5-3-5	4 mo	Patent
O	5-3-5	4 mo	Patent
P	5-3-5	6 mo	Patent

[a] End-central-end graft internal diameters in millimeters.

anastomotic sites would admit a 4 mm probe. In the case of the 6-4-6 mm double taper, the central portion would still admit a 4 mm probe, while a 5 mm dilator could be passed at both suture lines three to six months postoperatively. In general, there appeared to be more buildup of tissue at the pulmonary artery end of the graft than at the aortic end.

Group B (Aorta–Iliac Artery Grafts in Dogs)

Femoral pulses of equal intensity and good quality were palpable bilaterally in 4 of the 5 dogs up to the time of sacrifice. Examination of the tapered grafts positioned between the aorta and iliac artery in the dogs at the time of sacrifice three to six months postoperatively revealed that 4 of the 5 grafts were patent. The fifth was filled with an organized thrombus (Table 4). In these 5-3-5 mm tapered grafts it was possible to pass a 2 mm dilator through the central portion of the graft and a 4 mm probe at the anastomotic site in 3 of the animals, and a 3 mm probe at the central portion of the fourth one at the time of elective sacrifice.

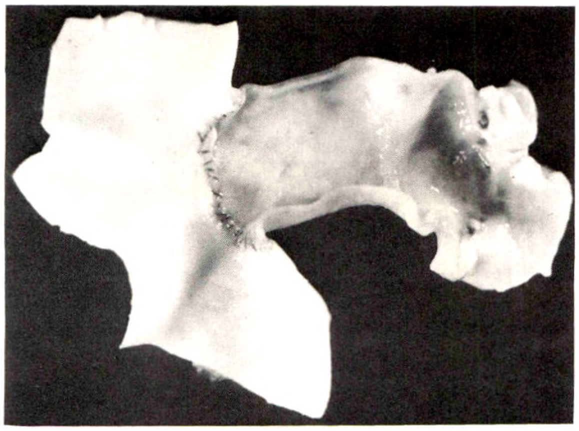


Fig 2. Gross pathological appearance of a doubly tapered graft six months following implantation between the pulmonary artery and descending aorta of a rhesus monkey. The ultrathin, glistening neointimal lining is evident throughout.

A comparison of the gross pathological findings in the two animal species revealed that they were similar, although the neointimal layer that developed tended to be somewhat thicker in the mongrel dogs after comparable periods of implantation. A thin, glistening pseudoendothelial covering was evident throughout the length of the graft. The anastomotic sites were well healed.

In the primate specimens histological examination of sections of the PTFE grafts prepared with hematoxylin-eosin and trichrome stains revealed the presence of a platelet-fibrin deposit filling the internodal spaces three months following implantation (Fig 3A). In some areas, particularly near the anastomotic sites and where adjacent areolar tissue was adherent to the graft, fibroblastic infiltration into the micropores was more advanced (Fig 3B). Even as late as six months postoperatively, organization of the deposit was not complete in primates, especially toward the center of the graft. Flattened pseudoendothelial cells could be seen on the surface facing the bloodstream over portions but not all of the inner surface of the material (Fig 4). The thickness of the inner tissue layer, while only one to several layers in depth in some areas (Fig 5A), tended to show increased buildup in other areas in which the original platelet fibrin deposit was more generous (Fig 5B).

The process was similar microscopically in the tapered grafts placed from the aorta to the iliac artery of the dogs except that the process of organization was always complete by three months. Cellular infiltration into the internodal spaces and thickness of the inner layer tended to be more generous at comparable periods of time.

Comment

The fabrication techniques used in construction of the expanded PTFE grafts offer several advantages. Not only can the pore size be regulated precisely, thereby encouraging the development of ultrathin neointimal lining [2, 5], but the configuration of the graft can be controlled at the same time. This allows a graft to be constructed that has a different lumen diameter in the central portion and at each end without producing any irregularity on the inner surface of the graft. In the initial series of experiments two sizes were used: the 5-3-5 mm tapered graft, which is intended for the construction of a systemic–pulmonary artery anastomosis in neonates, and

Table 4. Results following Insertion of a Doubly Tapered Graft from the Abdominal Aorta to the Iliac Artery in Mongrel Dogs

Dog	Configuration	Duration of Implantation	Findings
1	5-3-5[a]	3 mo	Occluded
2	5-3-5	3 mo	Patent
3	5-3-5	3 mo	Patent
4	5-3-5	3 mo	Patent
5	5-3-5	3 mo	Patent

[a] End-central-end graft internal diameters in millimeters.

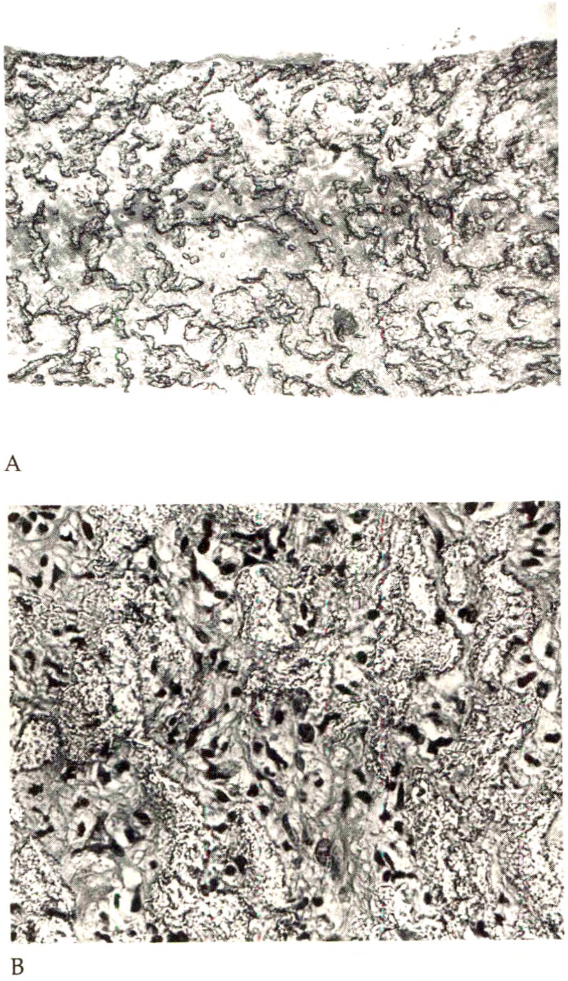


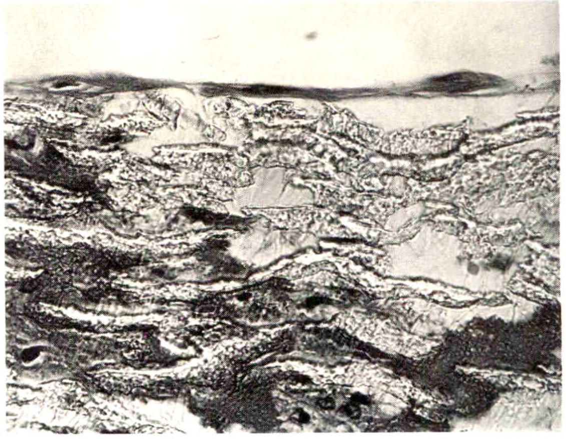
Fig 3. (A) Histological appearance of a doubly tapered graft three months following implantation in a rhesus monkey. The presence of a platelet-fibrin deposit filling the internodal spaces is evident. (B) In some areas fibroblastic infiltration into the spaces of the pores is evident (H&E; original magnification ×200.)

the 6-4-6 mm graft, which is designed for use in infants over 4 weeks of age.

Whereas the graft connected the aorta with the left pulmonary artery in these experiments, in a clinical setting it could be used in a variety of locations, for example, as a central shunt between the ascending aorta and the main pulmonary artery. Additionally, the configuration of a graft could be modified in a variety of ways depending on the anatomical requirements of a given situation. Thus, the central portion can be lengthened or shortened and the diameter of the end intended for anastomosis to the thin pulmonary artery can be made smaller than the diameter of the end to be sutured to the thicker aorta, producing, for example, a graft with internal diameters of 5 mm at one end, 3 mm centrally, and 4 mm at the other end. In this set of experiments the diameter of the central lumen chosen for construction of the grafts was selected in keeping with extensive clinical experience, which suggests that the diameter of an anastomotic channel that provides sufficiently increased blood flow to the pulmonary artery in a cyanotic baby while at the same time avoiding congestive heart failure is in the range of 3 mm for the neonate and 4 mm for the older infant [3, 4, 6, 7, 9].

It is important to note that some degree of tension on the graft was associated with a significant improvement in patency rate. If the graft was allowed to develop a degree of slack or if a kink developed along the length, a nidus for increased platelet-fibrin deposit was created with consequent thrombotic occlusion. This finding contrasts with the situation when autogenous saphenous vein bypass grafts are used in coronary artery bypass operations. Under this latter circumstance, veins tend to take a natural curvature when there is any degree of slack, probably because of the increased pliability of natural tissue. The grafts fabricated of expanded PTFE, on the other hand, while relatively pliable in comparison with most synthetic blood vessel substitutes, become somewhat stiffer than

Fig 4. Histological appearance of a tapered graft six months following implantation in a rhesus monkey. Flattened pseudoendothelial cells can be seen on the inner surface in some areas. (H&E; original magnification ×200.)



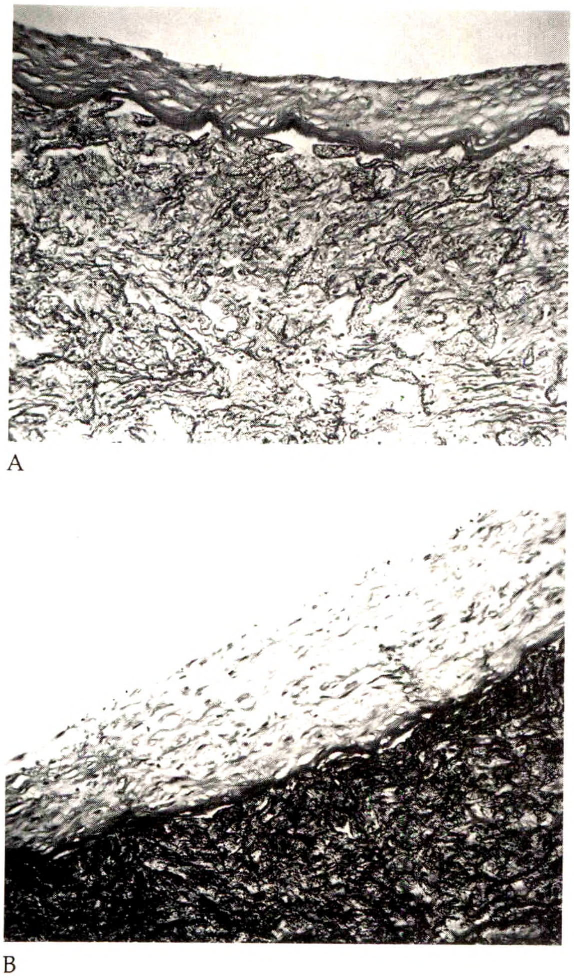


Fig 5. (A) The thickness of the inner cellular lining of the tapered grafts, while only one to several layers in depth in some areas six months following implantation in the primate, tended to show increased buildup in other areas (B) when the original platelet fibrin deposit was more generous. (H&E; original magnification ×200.)

natural tissue after implantation in the body as the internodal spaces become filled with platelet-fibrin deposit or connective tissue.

When the findings were compared with those noted in grafts of similar construction fabricated as straight grafts, the use of a double-taper configuration, at least in the dimensions used in these experiments, did not seem to be associated in itself with changes in blood flow that would increase the likelihood of thrombosis. Analysis of the data suggested that this may be due in part to the fact that some narrowing of the lumen at an anastomotic site coincident with the technical manipulations necessary for the completion of the anastomosis occurs more often than the surgeon realizes when suturing vessels of small diameter. Thus, it can be expected that when healing is complete in any straight graft, the lumen of the channel at the site of anastomosis will often be narrowed by a millimeter or so more than the lumen at the central portion of the graft, creating in effect a reverse taper after several months in the body. In this study the taper is being used to provide a technical advantage to the surgeon carrying out an anastomosis on a tube of very small dimensions in an effort to increase the diameter of the lumen at the site of anastomosis and thereby improve the patency rate.

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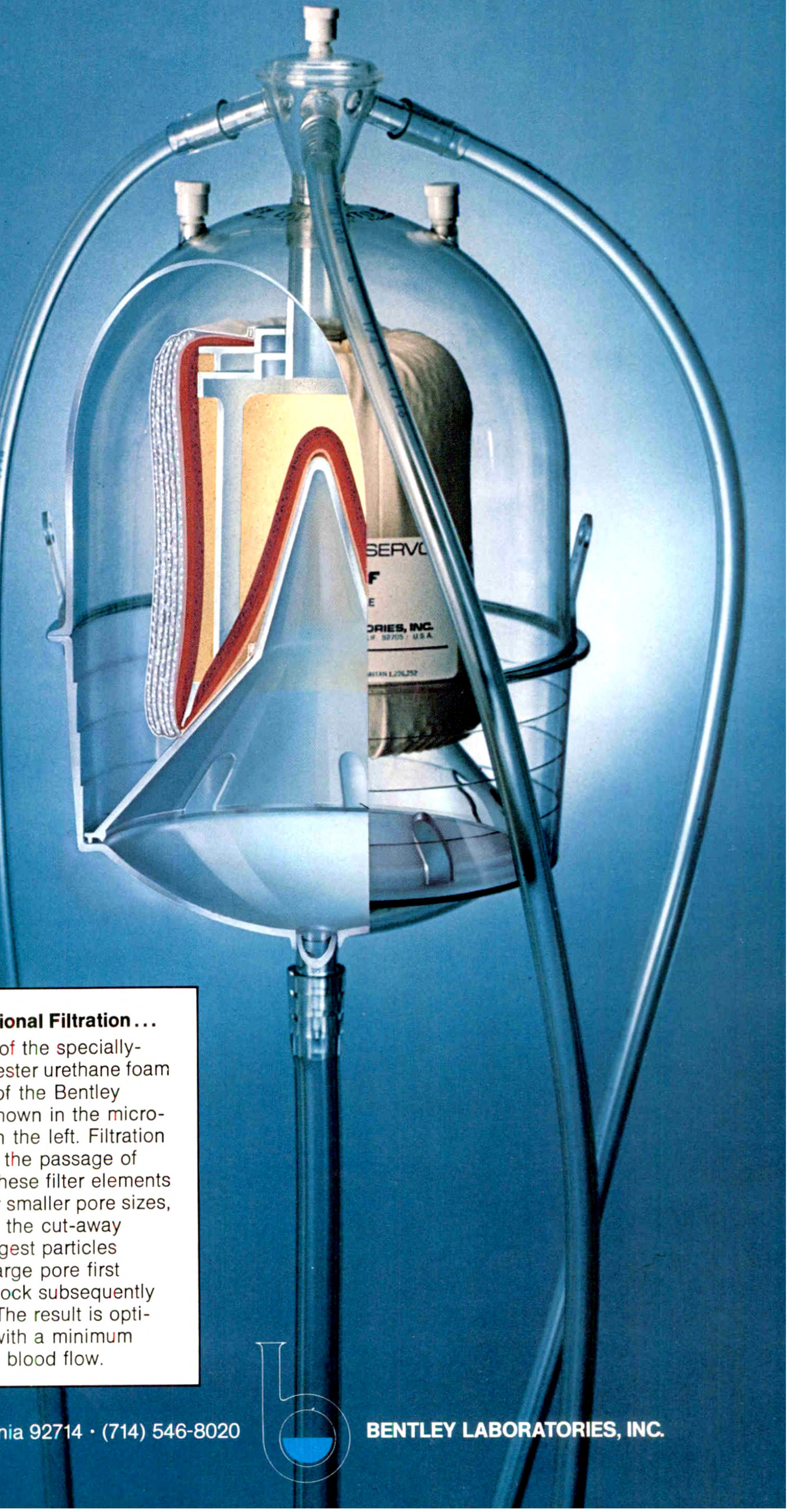

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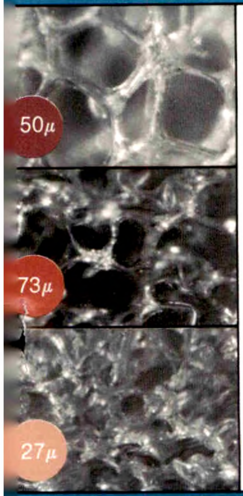

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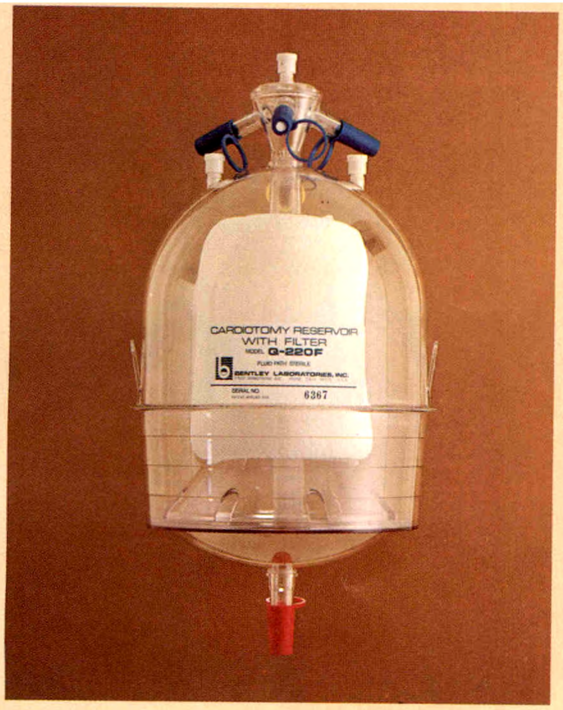

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The Q-220F Expanded Volume Cardiotomy Reserv
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- **Fast Set-up** No in-line filters to hook up; blood storage and filtration are handled by single unit.
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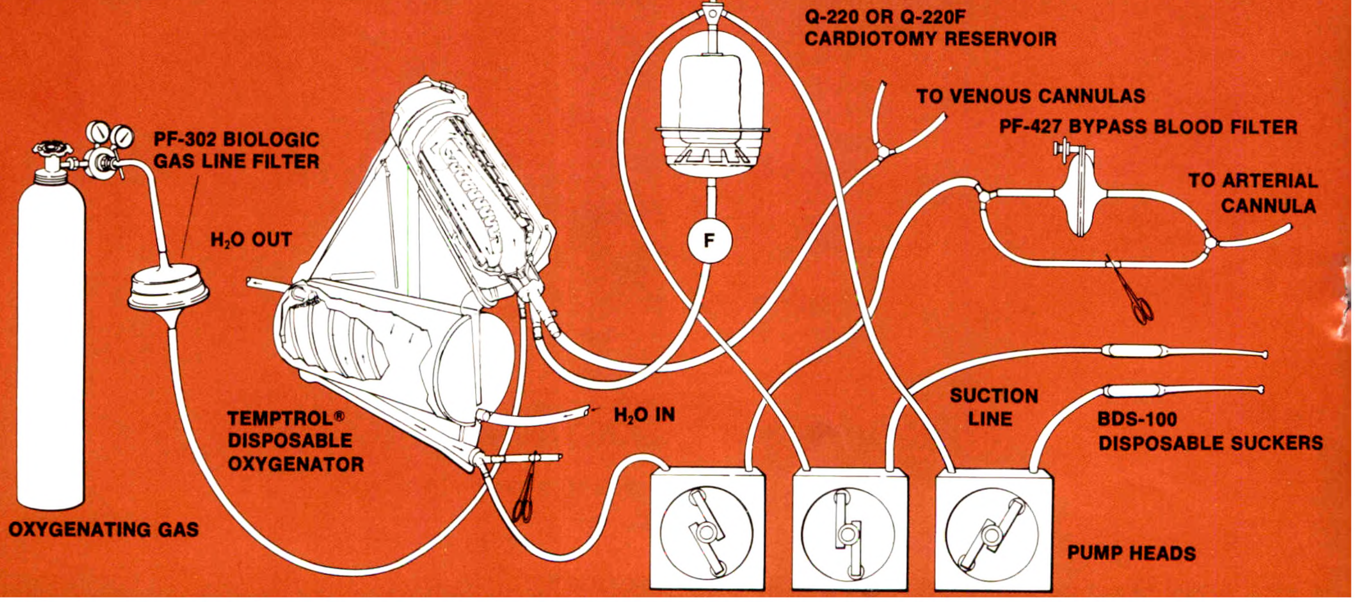
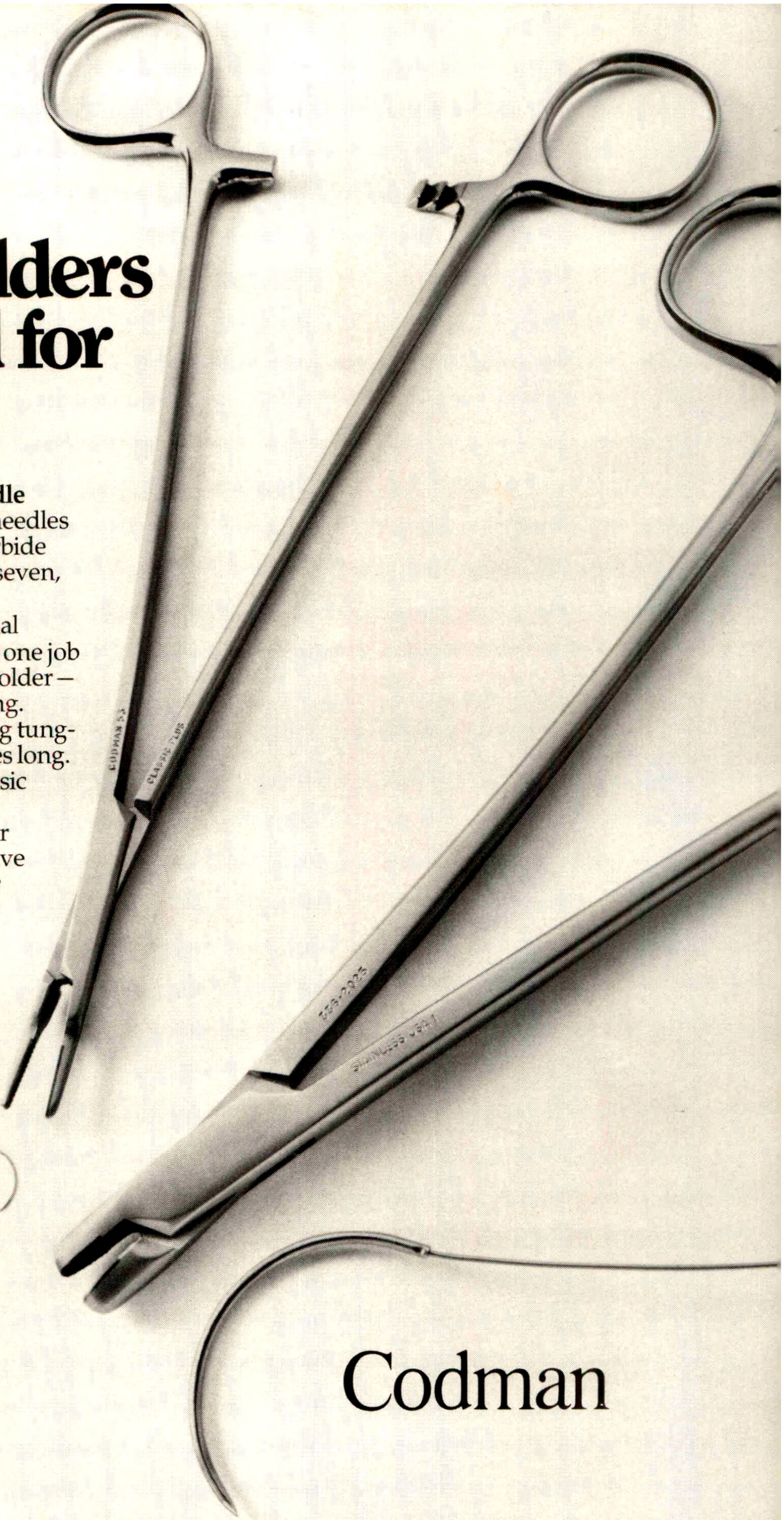
Now you can select the system best suited to the individual patient's needs. Bentley also manufactures the Q-220 Cardiotomy Reservoir. Identical to the Q-220F in outward appearance, the Q-220 does not contain a PolyFilter, but does incorporate a nylon tricot 110 micron filter. The letter "F" in the system diagram below represents the location of a Bentley PF-427 PolyFilter Bypass Blood Filter in the return line, should filtration be required when using the Q-220 Cardiotomy Reservoir. ☐ Bentley Cardiotomy Reservoirs are packaged and shipped sterile, ready to use.

The Bentley Extracorporeal System for Cardiopulmonary Bypass





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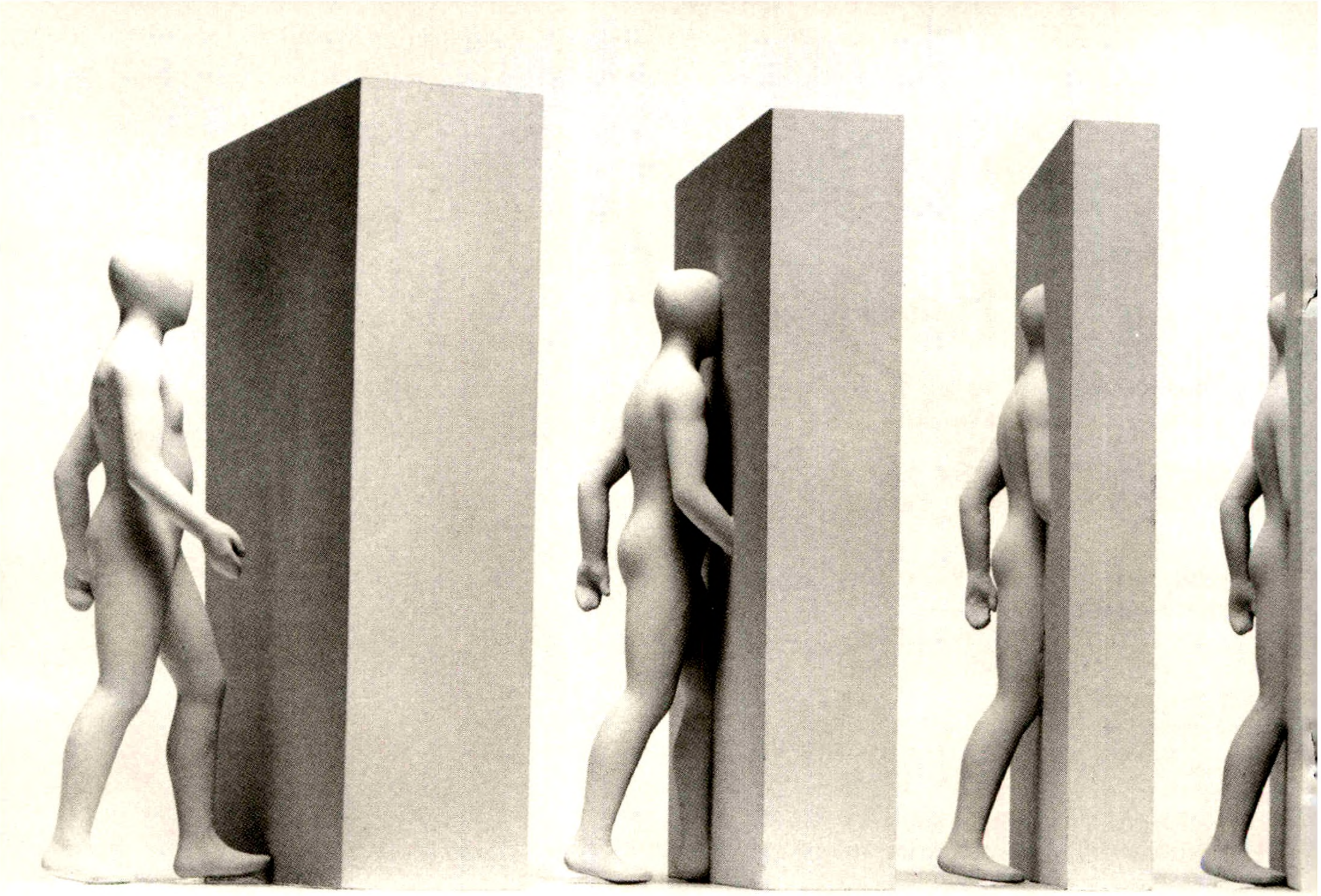


When the emergency of septic shock squeezes minutes into seconds

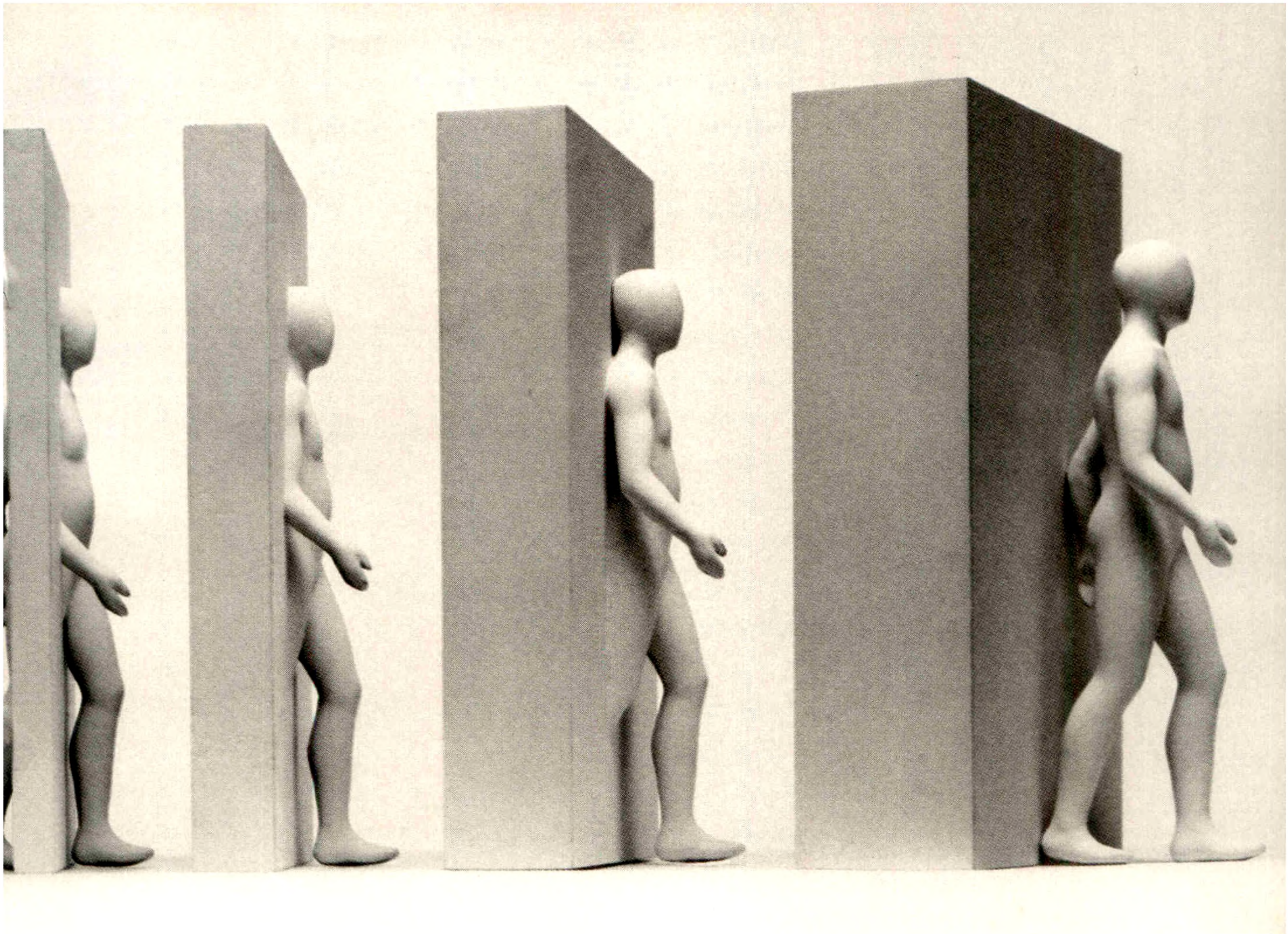
INTROPIN®

(dopamine HCl)

helps maintain kidney and mesenteric perfusion

Septic shock: rapid, progressive deterioration; immediate therapeutic measures to reverse the trend

With the onset of septic shock, it i generally agreed that the patient i in a state of rapid and progressive deterioration. Prognosis is grave, and the demand is for immediate therapy to reverse the trend.



Intropin (dopamine HCl): for the maintenance of vital organ perfusion

Intropin, a recently introduced catecholamine, is recommended as a significant adjunct to volume replacement, antibiotic therapy and other commonly accepted measures employed early in the treatment of septic shock.

In the low dosage range, Intropin generally produces an increase in kidney perfusion and urine output.

Intropin may also increase blood flow to the mesenteric beds while decreasing circulation to non-vital peripheral vascular beds. This favorable increase in vital organ perfusion at the expense of less important areas is a characteristic of Intropin, but not of other catecholamines.

Intropin: increases cardiac output and blood pressure

If adequate circulating blood volume is not restored in septic shock, cardiac output may fall with a resultant decrease in blood pressure.

Intropin substantially increases cardiac output by acting on the beta receptors of the heart. Low-to-moderate doses of Intropin are usually sufficient to manage hypotension due to inadequate cardiac output, and at these doses, Intropin increases blood flow to vital organs without increasing total peripheral vascular resistance.

Intropin: dosage phenomenon

Before administering Intropin, the physician should be familiar with the effects of the drug at various dose levels (see full prescribing information). Note especially the paradoxical results at the higher ranges (over 30 mcg/kg/min)—increased systemic vascular resistance plus a decrease in renal blood flow and urine output. These phenomena can be reversed, if desired, by reducing the dose.

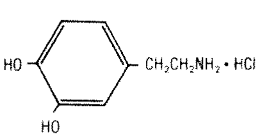
The half-life of Intropin is approximately 1.75 minutes, and the positive effects of the drug usually dissipate within 10 minutes after discontinuing the medication.

See following page of this advertisement for full prescribing information.

INTROPIN® (dopamine HCl)

5 ml. AMPUL/FOR I.V. INJECTION

DESCRIPTION: INTROPIN (dopamine HCl) is 3, 4-dihydroxyphenethylamine hydrochloride, a naturally-occurring biochemical catecholamine precursor of norepinephrine. The chemical structure is:



$C_8H_{11}NO_2 \cdot HCl$ Mol. Wt. 189.65

Dopamine hydrochloride is a white, odorless crystalline powder, freely soluble in water and soluble in alcohol. It is sensitive to light, alkalis, iron salts and oxidizing agents.

Each milliliter of sterile, pyrogen-free INTROPIN Injection contains 40 mg. of dopamine hydrochloride (equivalent to 32.96 mg. of dopamine base) in Water for Injection, USP, containing 1% sodium bisulfite as a preservative.

ACTIONS: INTROPIN exerts an inotropic effect on the myocardium resulting in an increased cardiac output. INTROPIN produces less increase in myocardial oxygen consumption than isoproterenol and its use is usually not associated with a tachyarrhythmia. Clinical studies indicate that INTROPIN usually increases systolic and pulse pressure with either no effect or a slight increase in diastolic pressure. Total peripheral resistance at low and intermediate therapeutic doses is usually unchanged. Blood flow to peripheral vascular beds may decrease while mesenteric flow increases. INTROPIN has also been reported to dilate the renal vasculature presumptively by activation of a "dopaminergic" receptor. This action is accompanied by increases in glomerular filtration rate, renal blood flow, and sodium excretion. An increase in urinary output produced by dopamine is usually not associated with a decrease in osmolality of the urine.

INDICATIONS: INTROPIN is indicated for the correction of hemodynamic imbalances present in the shock syndrome due to myocardial infarctions, trauma, endotoxic septicemia, open heart surgery, renal failure, and chronic cardiac decompensation as in congestive failure.

Where appropriate, restoration of blood volume with a suitable plasma expander or whole blood should be instituted or completed prior to administration of INTROPIN.

Patients most likely to respond adequately to INTROPIN are those in whom physiological parameters, such as urine flow, myocardial function, and blood pressure, have not undergone profound deterioration. Multiclinic trials indicate that the shorter the time interval between onset of signs and symptoms and initiation of therapy with volume correction and INTROPIN, the better the prognosis.

Poor Perfusion of Vital Organs – Urine flow appears to be one of the better diagnostic signs by which adequacy of vital organ perfusion can be monitored. Nevertheless, the physician should also observe the patient for signs of reversal of confusion or comatose condition. Loss of pallor, increase in toe temperature, and/or adequacy of nail bed capillary filling may also be used as indices of adequate dosage. Clinical studies have shown that when INTROPIN is administered before urine flow has diminished to levels approximately 0.3 ml./minute, prognosis is more favorable. Nevertheless, in a number of oliguric or anuric patients, administration of INTROPIN has resulted in an increase in urine flow which in some cases reached normal levels. INTROPIN may also increase urine flow in patients whose output is within normal limits and thus may be of value in reducing the degree of pre-existing fluid accumulation. It should be noted that at doses above those optimal for the individual patient, urine flow may decrease, necessitating reduction of dosage. Concurrent administration of INTROPIN and diuretic agents may produce an additive or potentiating effect.

Low Cardiac Output – Increased cardiac output is related to INTROPIN's direct inotropic effect on the myocardium. Increased cardiac output at low or moderate doses appears to be related to a favorable prognosis. Increase in cardiac output has been associated with either static or decreased systemic vascular resistance (SVR). Static or decreased SVR associated with low or moderate increments in cardiac output is believed to be a reflection of differential effects on specific vascular beds with increased resistance in peripheral beds (e.g. femoral) and concomitant decreases in mesenteric and renal vascular beds. Redistribution of blood flow parallels these changes so that an increase in cardiac output is accompanied by an increase in mesenteric and renal blood flow. In many instances the renal fraction of the total cardiac output has been found to increase. Increase in cardiac output produced by INTROPIN is not associated with substantial decreases in systemic vascular resistance as may occur with isoproterenol.

Hypotension – Hypotension due to inadequate cardiac output can be managed by administration of low to moderate doses of INTROPIN, which have little effect on SVR. At high therapeutic doses, INTROPIN's alpha adrenergic activity becomes more prominent and thus may correct hypotension due to diminished SVR. As in the case of other circulatory decompensation states, prognosis is better in patients whose blood pressure and urine flow have not undergone profound deterioration. Therefore, it is suggested that the physician administer INTROPIN as soon as a definite trend toward decreased systolic and diastolic pressure becomes evident.

CONTRAINDICATIONS: INTROPIN should not be used in patients with pheochromocytoma.

WARNINGS: INTROPIN should not be administered in the presence of uncorrected tachyarrhythmias or ventricular fibrillation.

Do **NOT** add INTROPIN to any alkaline diluent solution, since the drug is inactivated in alkaline solution.

Patients who have been treated with monamine oxidase (MAO) inhibitors prior to the administration of INTROPIN will require substantially reduced dosage. Dopamine is metabolized by MAO, and inhibition of this enzyme prolongs and potentiates the effect of INTROPIN. The starting dose in such patients should be reduced to at least one-tenth (1/10) of the usual dose.

Usage in Pregnancy – Animal studies have revealed no evidence of teratogenic effects from INTROPIN. In one study, administration of INTROPIN to pregnant rats resulted in a decreased survival rate of the newborn and a potential for cataract formation in the survivors. The drug may be used in pregnant women when, in the judgment of the physician, the expected benefits outweigh the potential risk to the fetus.

Usage in Children – The safety and efficacy of this drug in children has not been established. INTROPIN has been used in a limited number of pediatric patients, but such use has been inadequate to fully define proper dosage and limitations for use. Further studies are in progress.

PRECAUTIONS: Avoid Hypovolemia – Prior to treatment with INTROPIN, hypovolemia should be fully corrected, if possible, with either whole blood or plasma as indicated.

Decreased Pulse Pressure – If a disproportionate rise in the diastolic pressure (i.e. a marked decrease in the pulse pressure) is observed in patients receiving INTROPIN, the infusion rate should be decreased and the patient observed carefully for further evidence of predominant vasoconstrictor activity, unless such an effect is desired.

Extravasation – INTROPIN should be infused into a large vein whenever possible to prevent the possibility of extravasation into tissue adjacent to the infusion site. Extravasation may cause necrosis and sloughing of surrounding tissue. Large veins of the antecubital fossa are preferred to veins in the dorsum of the hand or ankle. Less suitable infusion sites should be used only if the patient's condition requires immediate attention. The physician should switch to more suitable sites as rapidly as possible. The infusion site should be continuously monitored for free flow.

Occlusive Vascular Disease – Patients with a history of occlusive vascular disease (for example, atherosclerosis, arterial embolism, Raynaud's disease, cold injury, diabetic endarteritis, and Buerger's disease) should be closely monitored for any changes in color or temperature of the skin in the extremities. If a change in skin color or temperature occurs and is thought to be the result of compromised circulation to the extremities, the benefits of continued INTROPIN infusion should be weighed against the risk of possible necrosis. This condition may be reversed by either decreasing or discontinuing the rate of infusion.

IMPORTANT – Antidote for Peripheral Ischemia: To prevent sloughing and necrosis in ischemic areas, the area should be infiltrated as soon as possible with 10 to 15 ml. of Saline solution containing from 5 to 10 mg. of Regitine® (brand of phentolamine), an adrenergic blocking agent. A syringe with a fine hypodermic needle should be used, and the solution liberally infiltrated throughout the ischemic area. Sympathetic blockade with phentolamine causes immediate and conspicuous local hyperemic changes if the area is infiltrated within 12 hours. Therefore, phentolamine should be given as soon as possible after the extravasation is noted.

Avoid Cyclopropane or Halogenated Hydrocarbon Anesthetics – Cyclopropane or halogenated hydrocarbon anesthetics increase cardiac autonomic irritability and therefore may sensitize the myocardium to the action of certain intravenously administered catecholamines. This interaction appears to be related both to pressor activity and to beta adrenergic stimulating properties of these catecholamines. Therefore, as with certain other catecholamines, and because of the theoretical arrhythmogenic potential, INTROPIN should be used with EXTREME CAUTION in patients inhaling cyclopropane or halogenated hydrocarbon anesthetics.

Careful Monitoring Required – Close monitoring of the following indices – urine flow, cardiac output and blood pressure – during INTROPIN infusion is necessary as in the case of any adrenergic agent.

ADVERSE REACTIONS: The most frequent adverse reactions observed in clinical evaluation of INTROPIN included ectopic beats, nausea, vomiting, tachycardia, anginal pain, palpitation, dyspnea, headache, hypotension, and vasoconstriction. Other adverse reactions which have been reported infrequently were aberrant conduction, bradycardia, piloerection, widened QRS complex, azotemia, and elevated blood pressure.

DOSAGE AND ADMINISTRATION:

WARNING: This is a potent drug: It must be diluted before administration to patient.

Suggested Dilution – Transfer contents of one ampul (5 ml. containing 200 mg. INTROPIN) by aseptic technique to either a 250 ml. or 500 ml. bottle of one of the following sterile intravenous solutions:

1) Sodium Chloride Injection, USP
2) Dextrose 5% Injection, USP
3) Dextrose (5%) and Sodium Chloride (0.9%) Injection, USP
4) 5% Dextrose in 0.45% Sodium Chloride Solution
5) Dextrose (5%) in Lactated Ringer's Solution
6) Sodium Lactate (1/6 Molar) Injection, USP
7) Lactated Ringer's Injection, USP

These dilutions will yield a final concentration for administration as follows:
250 ml. dilution contains 800 mcg./ml. of INTROPIN
500 ml. dilution contains 400 mcg./ml. of INTROPIN

INTROPIN has been found to be stable for a minimum of 24 hours after dilution in the sterile intravenous solutions listed above. However, as with all intravenous admixtures, dilution should be made just prior to administration.

Do **NOT** add INTROPIN Injection to 5% Sodium Bicarbonate or other alkaline intravenous solutions, since the drug is inactivated in alkaline solution.

Rate of Administration – INTROPIN, after dilution, is administered intravenously through a suitable intravenous catheter or needle. An i.v. drip chamber or other suitable metering device is essential for controlling the rate of flow in drops/minute. Each patient must be individually titrated to the desired hemodynamic and/or renal response with INTROPIN. In titrating to the desired increase in systolic blood pressure, the optimum dosage rate for renal response may be exceeded, thus necessitating a reduction in rate after the hemodynamic condition is stabilized.

Adminstration at rates greater than 50 mcg./kg./min. have safely been used in advanced circulatory decompensation states. If unnecessary fluid expansion is of concern, adjustment of drug concentration may be preferred over increasing the flow rate of a less concentrated dilution.

Suggested Regimen:

1. When appropriate, increase blood volume with whole blood or plasma until central venous pressure is 10 to 15 cm H_2O or pulmonary wedge pressure is 14-18 mm Hg.

2. Begin administration of diluted solution at doses of 2-5 mcg./kg./minute INTROPIN in patients who are likely to respond to modest increments of heart force and renal perfusion.

In more seriously ill patients, begin administration of diluted solution at doses of 5 mcg./kg./minute INTROPIN and increase gradually using 5 to 10 mcg./kg./minute increments up to 20 to 50 mcg./kg./minute as needed. If doses of INTROPIN in excess of 50 mcg./kg./minute are required, it is suggested that urine output be checked frequently. Should urine flow begin to decrease in the absence of hypotension, reduction of INTROPIN dosage should be considered. Multiclinic trials have shown that more than 50% of the patients were satisfactorily maintained on doses of INTROPIN less than 20 mcg./kg./minute. In patients who do not respond to these doses with adequate arterial pressures or urine flow, additional increments of INTROPIN may be employed in an effort to produce an appropriate arterial pressure and central perfusion.

3. Treatment of all patients requires constant evaluation of therapy in terms of the blood volume, augmentation of myocardial contractility, and distribution of peripheral perfusion. Dosage of INTROPIN should be adjusted according to the patient's response, with particular attention to diminution of established urine flow rate, increasing tachycardia or development of new dysrhythmias as indices for decreasing or temporarily suspending the dosage.

4. As with all potent intravenously administered drugs, care should be taken to control the rate of administration so as to avoid inadvertent administration of a bolus of drug.

OVERDOSAGE: In case of accidental overdosage, as evidenced by excessive blood pressure elevation, reduce rate of administration or temporarily discontinue INTROPIN until patient's condition stabilizes. Since INTROPIN's duration of action is quite short, no additional remedial measures are usually necessary. If these measures fail to stabilize the patient's condition, use of the short-acting alpha adrenergic blocking agent, phentolamine, should be considered.

HOW SUPPLIED: 5 ml. ampuls containing 40 mg. dopamine HCl per milliliter. September, 1975

ARNAR-STONE LABORATORIES, INC.
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The Operative Problem of Small Left Atrium in Total Anomalous Pulmonary Venous Connection: Report of 5 Patients

Daniel A. Goor, M.D., Alon Yellin, M.D., Mira Frand, M.D.,
Aram Smolinsky, M.D., and Henry N. Neufeld, M.D.

ABSTRACT **A moderately small left atrium is a common finding in total anomalous pulmonary venous connection (TAPVC). In most patients in whom the common pulmonary vein is anastomosed to the left atrium, the small size of this chamber does not interfere with good operative results. Recently a patient was encountered in whom the left atrium measured less than 2 cm in its greatest dimension. This atrium was too small to take an anastomosis with the common pulmonary vein. Therefore the common pulmonary vein was anastomosed primarily to the right atrium, the floor of the fossa ovalis was excised, and a pericardial conduit was constructed. Subsequently, 4 additional patients have been similarly treated. The problem of small left atrium in TAPVC is discussed.**

The problem of a small left atrium in total anomalous pulmonary venous connection (TAPVC) has been described in the past [1, 3–5, 9, 11], but its operative implications have received only scant attention [1, 3]. Recently we operated on a 2-year-old child in whom the left atrium was too small to take an anastomosis with the common pulmonary vein. It was necessary to develop a specific technique for overcoming the problem. Subsequently 4 additional patients with similar anatomical findings have been treated. These 5 cases are described and discussed.

Case Histories

Patient 1

A 2-year-old boy had first been admitted to this hospital at the age of 4 months because of suspected pneumonia with diarrhea. Physical examination at that time revealed mild cyanosis, right ventricular heave, a grade 3/6 systolic murmur along the left sternal border, a diastolic flow murmur over the tricuspid area, fixed splitting of the second heart sound, and accentuated P_2. The electrocardiogram showed an axis of +120 degrees with marked right ventricular hypertrophy and incomplete right bundle-branch block. Chest roentgenograms revealed cardiomegaly and increased pulmonary vascular markings. Catheterization data are shown in the Table. Cineangiography demonstrated a common pulmonary vein draining through a vertical vein to the innominate vein. The patient was treated with digitalis and diuretics, and at the age of 2 years, at a body weight of 8 kg, he underwent operative repair of the malformation.

The operation was performed at 32°C through a midsternotomy approach. A transverse incision was made beginning on the anterior wall of the right atrium and extending through the back wall and the atrial septum to the back wall of the left atrium (Figure). An incompetent patent foramen ovale measuring about 5 mm in diameter was seen. The left atrium was extremely small, measuring 2 cm in the longest dimension. The mitral valve was found to lie against the atrial septum.

The floor of the fossa ovalis was excised. An incision measuring 6 cm in length was made along the common pulmonary vein. The right end of this incision was at the bifurcation of the common pulmonary vein at the right hilus. Since the left atrium measured about 2 cm in its longest dimension, about two-thirds of the common pulmonary vein was anastomosed to the right atrium and only one-third to the left atrium (see the Figure). Following that, a pericardial patch was sutured along the fossa

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Preoperative and Postoperative Catheterization Data in Patient 1

	Before Operation			After Operation		
	O_2 Sat (%)	Pressure (mm Hg)	Mean Pressure	O_2 Sat (%)	Pressure (mm Hg)	Mean Pressure
IVC	74.2			75.2		
SVC				80.8		
Right atrium						
High	91.8			77.5		
Middle	85.8	a = 10	6.5			
Low	88.0			77.0		
Right ventricle						
Tricusp	79.2					
Body	83.8	75/22		77.0	30/0–5	
Outflow	84.3	110/0				
MPA				73.5	25/5	20
LPA				62.0	25/15	20
LA	84.3	a = 7	4			
Subclavian artery	64.0			97.0		

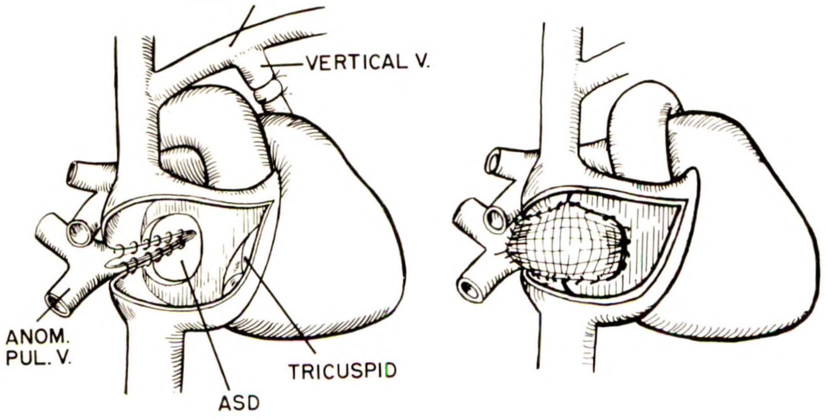
ovalis and the line of anastomosis so that all of the pulmonary venous blood drained to the left atrium (see the Figure). The anastomosis and the patch were constructed through the interior of the right atrium. No technical difficulties were encountered. As a consequence of this patching, the middle third of the sinus intercavarum of the right atrium became a functional part of the left atrium.

Total bypass time was 47 minutes. There were no immediate problems postoperatively, and his course was surprisingly smooth. He was discharged on the tenth postoperative day.

About ten months after this operation elective heart catheterization was done (see the Table). At that time the boy appeared to be in excellent health, was taking no medications, and weighed 13 kg. Physical examination revealed a grade 2/6 systolic murmur over the pulmonary valve area. The electrocardiogram showed an axis of +75 degrees, incomplete right bundle-branch block, and no evidence of ventricular hypertrophy.

Patient 2

A 5-year-old girl who had a supracardiac type of TAPVC draining into the innominate vein underwent an operation identical to that per-



Operative technique. Through the opened right atrium and excised floor of the fossa ovalis, the common pulmonary vein is anastomosed to both atria. Patch closure is done and the midportion of the sinus intercavarum is excluded from the right atrium. (ASD = *atrial septal defect.)*

formed on Patient 1. Her left atrium, though, was only moderately small. She was discharged on the tenth postoperative day.

Patient 3

A 6-month-old boy who weighed 4.6 kg underwent emergency operation for general deterioration and active, nonresolving pneumonia. At operation it was found that his two right pulmonary veins were draining into the sinus intercavarum of the right atrium and the two left pulmonary veins into the coronary sinus. The left atrium was very small, and it was hard to compare it to a normal chamber.

The floor of the fossa ovalis was excised, and a patch was constructed so as to drain the pulmonary venous blood into the left atrium; in addition, the left atrium was enlarged. The operation was performed under moderately deep hypothermia (24°C) and total circulatory arrest for 20 minutes. Total bypass time (including arrest) was 40 minutes. The infant was discharged from the hospital on the seventeenth postoperative day.

Patient 4

A 4-year-old boy, 12 kg in weight, had a TAPVC into the coronary sinus in addition to tetralogy of Fallot. The tetralogy was corrected in the ordinary fashion. Repair of his TAPVC consisted of excision of the floor of the fossa ovalis as well as a large portion of the septum between the coronary sinus and the atrium. Then a patch septum was constructed as for Patient 3. The left atrium was only moderately small. Total bypass time was 70 minutes. The patient was discharged on the tenth postoperative day.

Patient 5

A 20-year-old man with supracardiac TAPVC draining into the innominate vein had an operation identical to that of Patient 1 and was discharged on the tenth postoperative day.

Comment

The operation used in these 5 cases is a further modification in the procedure of intracardiac repair [3, 6, 10, 15]. The technique is very similar to that used by Gersony and co-workers [6] except that the anastomosis had to be made with both atria. The concept of enlarging the left atrium is similar to that described by Cooley [3, 4] except that in our patients we achieved it by excising the floor of the fossa ovalis and constructing a pericardial conduit graft. By so doing, a relatively large part of the right atrium was added to the left atrium. We estimate that approximately the middle third of the sinus intercavarum of the right atrium was taken by the left atrium, and the larger part of the functional left atrium is derived from the right atrium.

The diminutive size of the left atrium in the first patient did not lend itself, we believe, to the left external approach recommended by Roe [14]. This is because the left atrium was not large enough to take an adequate anastomosis, nor, probably, was it large enough to function afterward as a left atrium.

Currently, although there has been a tremendous improvement in the results of operation for TAPVC, the mortality rate is still rather high. The operative mortality for patients above the age of 1 year is about 7% [7]; below 1 year it is between 10 and 20% [2, 12].

The crucial question is whether death may be due to a left atrium that is too small. We are not aware of any definitive study in which the size of the left atrium was measured and related to operative results. However, there is some indirect evidence that the size of the left atrium may play a role in the results of these operations, and therefore, if the chamber is properly repaired, some improvement in results can be expected.

Further supporting evidence for this has been provided by Keith and associates [11], who concluded that there is an absolute rather than a relative reduction in the size of the left atrium. Based on their pathological studies they believed that because of the small size of the left atrium, surgical correction of these malformations is not feasible. Apparently in their pathological experience they encountered extreme cases such as our first patient. However, severe hypoplasia of the left atrium is not a common finding.

During the preparation of a recent report [8] we studied 5 pathological specimens of TAPVC. In each of these there was an obvious reduction in the size of the left atrium, but in none was the left atrium nearly as small as in the first patient reported here. According to Gomes and associates [7], the operative mortality in their series was closely related to the size of the atrial septal defect (ASD). Of 11 patients whose ASD had a diameter smaller than 6 mm, 8 died. In patients whose ASD was larger than 6 mm, the mortality was negligible. Although it has not been proved, the assumption may be made that the smaller the ASD, the smaller the left atrium. Support for this view is found in the report of Miller and co-workers [13], in which balloon septostomy in infants with TAPVC resulted in an increase in the size of the left atrium. In a recent report by Appelbaum, Kirklin, and associates [1] the problem of the small left atrium is discussed, and it is stressed that the techniques used in the past to enlarge the size of the left atrium have been ineffective.

The crucial point of the technique described here is that an adequate anastomosis is first made between the atria and the common pulmonary vein. Once this is done, the surgeon can decide how much to take from the right atrium for the left atrium. This cannot be done from the right or left external approach, but only by the right atrial intracardiac approach.

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Pulmonary Venoocclusive Disease

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ABSTRACT **Pulmonary venoocclusive disease has been established as a definite clinical entity characterized by congestive cardiac failure with pulmonary arterial hypertension, chronic interstitial pulmonary edema, and normal wedge pressure on cardiac catheterization. This disease was diagnosed and confirmed in a patient during life. A review of the 32 patients reported earlier has been done in an attempt to find possible etiological agents. Early recognition and treatment with anticoagulants, methylprednisolone, aspirin, and dipyridamole may improve the prognosis.**

Pulmonary venoocclusive disease is a rare entity usually diagnosed at postmortem examination. As information about it has gradually increased [2, 4, 8], its clinical description has become established. We report here the third case in the literature diagnosed during life. Attempts to determine the etiology and to establish a treatment for this syndrome have been unsuccessful to date.

Case Report

A 19-year-old man was first seen at Rush-Presbyterian-St Luke's Hospital in August, 1972, with a history of dyspnea and epileptic seizures. Studies during an earlier admission at another hospital had included a normal brain scan and electroencephalogram. Treatment with dilantin and phenobarbital was started.

Physical examination showed that the patient was in no acute distress. There was no cyanosis, clubbing or prominence of neck veins. The lungs were clear. Cardiac examination revealed a normal first heart sound and a prominent pulmonary second sound with normal splitting. No cardiac murmurs were heard. The chest roentgenogram was unremarkable except for prominent pulmonary artery segments.

Cardiac catheterization revealed no intracardiac shunts. The right ventricular pressure was 44/6 mm Hg, and the pulmonary artery pressure was 43/26 mm Hg with a mean of 34 and increased with exercise to 56/32 mm Hg with a mean of 43. Pulmonary wedge pressure was 9 mm Hg and decreased to 7 mm Hg with exercise. Total pulmonary resistance was 105 dyne sec cm^{-5} with a pulmonary arteriolar resistance of 77 dyne sec cm^{-5}. The pulmonary angiogram was normal, with no evidence of left atrial obstruction.

The patient had been readmitted at another hospital in 1974 because of moderate dyspnea. His pulmonary function tests at that time were reported as normal, and no change in his chest roentgenogram was demonstrated.

The patient was admitted to our hospital for the first time on August 20, 1974, because of increased dyspnea and changes on his chest roentgenogram. He denied any history of cough, hemoptysis, weight loss, pneumonitis, chills, fever, hoarseness, chest discomfort, or wheezing. He smoked a pipe occasionally. Past history was not suggestive of rheumatic fever. There were no siblings in the family with similar pulmonary disease.

On physical examination his heart rate was 60/min and regular. The respiratory rate was 20/min, and blood pressure in the right upper arm was 90/60 mm Hg. At this admission he showed mild clubbing of the nailbeds and peripheral and circumoral cyanosis. The anteroposterior diameter of the chest was increased. No rales or wheezing were heard in the lungs. Evaluation of the cardiovascular system revealed normal jugular venous pressure, a pronounced right ventricular lift, normal first heart sound, and a loud, split pulmonary second sound. Again, no cardiac murmurs were heard. Abdominal examination showed a normal liver and enlarged spleen.

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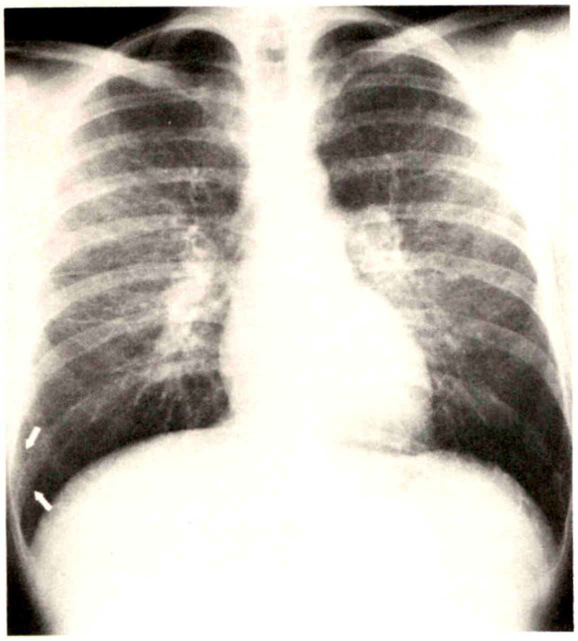
Laboratory data included a hemoglobin of 13.9 gm/100 ml, hematocrit of 40.8%, white blood cell count of 5,100/mm^3 with 61% polymorphonuclear leukocytes, 20% band forms, 8% monocytes, 7% lymphocytes, and 2% eosinophils. Platelets were normal. The liver profile was normal except for an alkaline phosphatase of 103 IU/liter (normal, 30 to 85). The electrocardiogram showed right axis deviation with right ventricular hypertrophy. A lupus erythematosus preparation and collagen profile were negative. Serum electrophoresis demonstrated a total protein of 7.2 gm/100 ml, albumin 3.8 gm/100 ml, and an alpha fraction of 0.3, beta of 0.9, and gamma of 1.4%. The toxoplasmosis titer was negative. Coagulation profile revealed a prothrombin time of 55% with partial thromboplastin time of 39 seconds. Bone marrow aspirate was within normal limits.

The chest roentgenogram (Fig 1) showed normal heart size, bilateral hilar prominence, a diffuse bilateral reticular nodular pattern, and the presence of Kerley B lines, indicative of interstitial edema.

The liver scan was normal. A spleen scan showed splenomegaly with maldistribution of the dye but no discrete lesions. Lung scan disclosed diffuse irregularity in pulmonary perfusion but no discrete defects. The pattern was suggestive of chronic lung disease (as opposed to pulmonary embolism). Pulmonary function tests revealed normal lung volumes, small airway obstruction, mild hypoxia for his age, and minimal restrictive disease. Oxygen saturation at room air was 90 mm Hg, which increased to 553 mm Hg on 100% oxygen. There were no detectable intracardiac shunts.

Fig 1. Chest roentgenogram showing normal-sized heart, bilateral hilar prominence, diffuse pulmonary reticular pattern, and Kerley B lines (arrows).

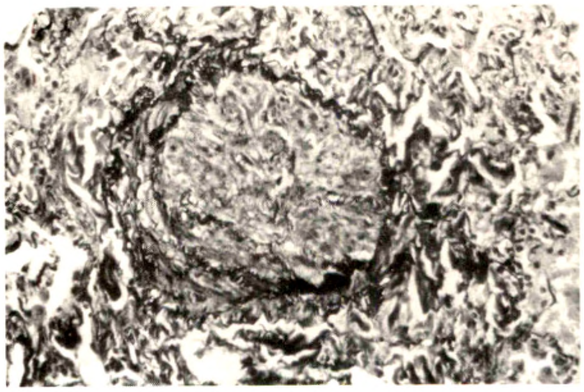


On August 21, 1974, mediastinoscopy revealed sinus histiocytosis of the paratracheal lymph nodes. A wedge lung biopsy was done a week later. The lungs showed a slight delay in collapse during expiration. On palpation there was a doughlike feeling suggestive of increased tissue resistance, more pronounced in some areas than others.

Microscopical examination revealed prominent venules markedly thickened by proliferating fibrous tissue (Fig 2). The majority of these vessels were located in the pulmonary parenchyma at some distance from the bronchiolar structures. The sclerotic process had significantly narrowed or totally obliterated the lumen (Fig 3). Scattered throughout the remaining parenchyma were focal collections of hemosiderin-laden macrophages. Foreign body giant cells were present that contained phagocytized fragments of fibrillar material demonstrated to be elastic fibers partially coated with iron pigment. There was no evidence of acute or chronic pneumonitis.

Heparin (4,000 units q6h) was given intrave-

Fig 2. Prominent venules markedly thickened by proliferating fibrous tissue that totally occludes the lumen. (Verhoeff elastic tissue stain, ×472.)



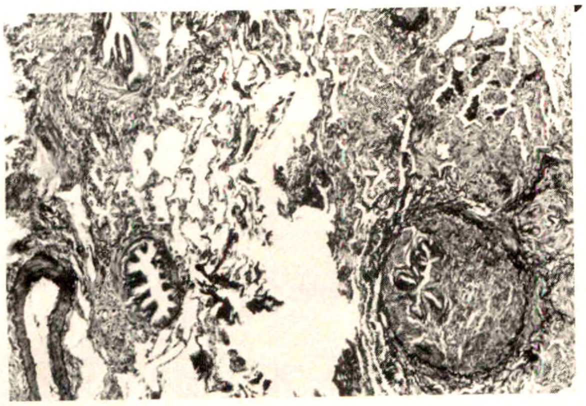


Fig 3. Intersegmental vein lying near a major bronchus and pulmonary artery. Note the patent pulmonary artery. The lumen of the pulmonary vein is narrowed by the sclerotic process. (Verhoeff elastic tissue stain, ×143.)

nously for ten days. This was later changed to warfarin. Simultaneously the patient was given prednisone (80 mg daily). He was discharged home on a regimen of warfarin, aspirin (1 gm daily), dipyridamole (100 mg daily), and methylprednisolone (30 mg daily). With this management he continued to do well two years after the onset of his symptoms.

Comment

This patient had a disease characterized by pulmonary hypertension, chronic pulmonary edema, normal pulmonary artery wedge pressure, and a lack of alveolar-capillary membrane diffusion block. Primary pulmonary hypertension due to either thromboembolic disease or so-called idiopathic pulmonary hypertension does not cause pulmonary edema. In far-advanced cases the lung fields tend to be more radiolucent than normal. The lack of pulmonary venous hypertension rules out the possibility of mitral stenosis, myxoma, proximal pulmonary vein stenosis, or myocarditis. The time course and clinical features differ from infiltrative pulmonary disease such as sarcoidosis, tuberculosis, eosinophilic granuloma, or Liebow's desquamative interstitial pneumonia. The roentgenographic picture might suggest lymphangitis carcinomatosa, but the fact that the clinical course lasted two years and that pulmonary hypertension developed as an initial finding did not support this diagnosis.

In summary, our patient showed a syndrome of pulmonary arterial and capillary hypertension (manifested by edema) without venous hypertension. The obstruction was at the level of venules, as confirmed at biopsy.

Clinical Features

Thirty-two patients have been described in the literature, and the findings are summarized in the Table. Adding our patient to this group, two-thirds of the 33 patients have been more than 16 years old. The majority were male. The chief symptoms were dyspnea and congestive heart failure. Cyanosis was present in almost half of the reported cases. Hemoptysis occurred but was rare as a presenting symptom. The physical findings, when described, were those of an increased right ventricular impulse and a loud pulmonary second sound. The electrocardiographic findings were right axis deviation with right ventricular hypertrophy and strain.

Radiological appearances are the most important findings in distinguishing venoocclusive disease from primary pulmonary hypertension. In both, the right ventricle is enlarged and the main pulmonary branches are dilated, but in primary pulmonary hypertension the peripheral lung fields appear oligemic [5]. By contrast, in venoocclusive disease there is increased prominence of the central pulmonary vasculature and the development of peripheral septal lines (Kerley B lines) [10]. A pulmonary arteriogram usually reveals dilated, patent pulmonary arteries, a markedly prolonged circulation time, and a normal left atrium and pulmonary veins [10].

At cardiac catheterization all reported patients showed moderate to severe pulmonary arterial hypertension and nearly normal pulmonary wedge pressure. Many authors [1, 11] mentioned difficulty in obtaining satisfactory wedge pressure tracings. The pulmonary wedge pressure was raised in 1 previous patient (mean of 18 mm Hg), though direct measurement of pressure in the left superior pulmonary vein at thoracotomy was only 6 mm Hg. An observation made by several authors [1, 8] may be pathognomonic of this disease: When the catheter is wedged directly into the area of venous obstruction, a wedge pressure is not recorded. When the wedged catheter is flushed through with

Data on the 33 Reported Patients with Pulmonary Venoocclusive Disease

			Symptoms			Cardiac Catheterization		Arterial Po_2 (mm Hg)				
Authors	No. of Patients	Age (yr), Sex	SOB	Hemoptysis	Cyanosis	PA Pressure (mm Hg)	PA Wedge Pressure (mm Hg)	Resting	100% O_2	Treatment	Hosp Course	Time of Diagnosis
Brown and Harrison [2], 1966	9	5 under 16; M, 6; F, 3	All	None	3	75–108/ 25–55	6–18	67.7	600	Heparin	6 days to 5 yr	2 antemortem, 7 postmortem
Liebow, 1967[a]	16	5 under 16; sex unknown	All	1	–	Elevated	Normal	...	...	Unknown	Unknown	Postmortem
Dainauskas et al [4], 1971	1	28, F	+	–	–	80/50	9	92.2	...	Heparin	5 mo	Postmortem
Heath et al [6], 1971	1	5, F	+	–	+	70/35	...	...	...	...	16 mo	Postmortem
Scheibel et al [10], 1972	2	45, M 32, M	+ +	– –	+ +	88/42 86/46	20 7	91 ...	... ...	Heparin, methylprednisolone	4 wk 8 wk	Postmortem Postmortem
Liebow et al [8], 1973	1	15, M	+	–	+	115/53	...	77	92	Heparin, methylprednisolone	...	Postmortem
Braun et al [1], 1973	1	34, M	+	+	+	$\overline{50}$	8	...	...	Heparin, methylprednisolone	8 days	Postmortem
Rosenthal et al [9], 1973	1	13, F	+	–	–	...	...	93	...	Heparin, methylprednisolone	48 days	Postmortem
Chawla et al (present case)	1	19, M	+	–	+	43/26	$\overline{9}$	90	553	Heparin, methylprednisolone, dipyridamole, aspirin	Alive 1 yr	Antemortem

[a] Liebow collected referral cases. Details not described.

SOB = shortness of breath; PA = pulmonary artery.

saline solution, pressure rises disproportionately and then falls extremely slowly to the base level. This is because saline is trapped between the thrombosed vein and the catheter tip.

Heparin (combined with methylprednisolone and digoxin) was the treatment of choice in the reported patients. Furosemide was given in 1 instance in a patient diagnosed during life. All the previously reported patients have died.

Pathological Findings

The pathological findings were discussed in 1934 by Höra [7] and have been reviewed by others. The primary lesion is described as an organizing thrombus in the small veins and venules. In our earlier patient [4] and the present one, no actual thrombi were encountered. As has been reported by others [1, 3], the lumens of medium-sized and small pulmonary veins were completely or almost completely obliterated by loosely arranged, proliferating connective tissue. The lesions are usually widespread and may involve any segment of the lungs. The term *endogenous pneumoconiosis* was devised by Liebow and associates [8] to signify this process of multiple foreign body giant cells containing phagocytized fragments of elastic fibers partially coated with iron pigment. Does this signify an active destructive process of the elastic tissues of the veins? Is this an inherent abnormality in the elastic tissues of the veins, an infective process, or an autoimmune disease? These and other questions remain to be answered.

No real etiological clue emerges from the case histories. A genetic role in the pathogenesis of the disease is suggested by the death of a sibling with the same disease and also because one-third of the patients are 16 years old or younger [9]. An infectious origin has been postulated [6, 11, 13], but attempts to isolate an organism or demonstrate a titer response to an infectious origin have been unsuccessful [11, 13, 14]. Panphlebitis [3], infectious granuloma [1], and toxoplasmosis [11] have been suggested. Tests for collagen disease and immunological abnormalities have uniformly been negative [1, 14], including the present case. Weisser and associates [14] have drawn an analogy between the obliterative pulmonary venous lesions and the obliteration of intrahepatic veins that occurs in the Budd-Chiari syndrome. In Jamaica and South Africa the liver diseases have been shown to be caused by *Senecio* alkaloids contained in certain "bush teas." This suggests the possibility of inhaled toxins as etiological agents. Disseminated intravascular coagulation or a hypercoagulable state [1] may be important in the pathogenesis of this disease, but only mild abnormalities of coagulation have been noted in the reported cases.

Since the etiology remains undetermined, treatment has been empirical. The so-called pulmonary edema characteristic of this condition has been treated with digoxin and furosemide. Methylprednisolone and heparin have generally been used. The ultimate fatal outcome indicates that none of the treatments has been effective.

Because the thrombotic process may add to further destruction of lung parenchyma, anticoagulation therapy has been, and should be, used. In addition to the usual anticoagulants, these patients should also receive aspirin and dipyridamole to inhibit platelet function. Endothelial lesions (if this process is "vasculitis") would enhance the platelet participation in further pathogenesis. Methylprednisolone should be given to deter the progression of vasculitis.

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Transaxillary Minithoracotomy: The Optimal Approach for Certain Pulmonary and Mediastinal Lesions

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ABSTRACT **This report concerns the use of transaxillary thoracotomy for a variety of pulmonary, pleural, and mediastinal conditions in 50 patients. Primary and metastatic carcinomas, pneumothoraces, and benign lesions such as bronchogenic cysts and neurogenic tumors can be identified, evaluated, and treated with confidence. Reduced postoperative pain and morbidity, rapid return of arm and shoulder movements, reduced hospital stay, and excellent cosmetic result are among the advantages of this approach when compared with the usual posterolateral thoracotomy.**

We wish to focus attention on a simplified approach for the precise identification, assessment, appropriate decision-making, and operative management of a diverse group of pulmonary and mediastinal lesions—the transaxillary approach [1]. No originality whatever is claimed for this approach; we have merely broadened its application to include a wider spectrum of disease processes that we believe can be approached easily and quickly and can be adequately identified and treated through a minimal incision and with rapid postoperative recovery, decreased morbidity, and minimal risk factors.

In the past few years our medical colleagues have coined the words *invasive* versus *noninvasive* techniques. Various alternatives to open thoracotomy for diagnosis of chest lesions have been developed and are gaining wide acceptance. We question whether some of these procedures are worth the time, effort, delay, and risk involved. We seriously challenge the benefit-yield results. We wish to report our experience with a minithoracotomy through the transaxillary route to demonstrate the flexibility of a surgical philosophy that is consistent with good results. It matters not whether a chest specialist is a surgeon, internist, or radiologist; what really matters is the ability of all of us to integrate all the modalities of pulmonary diagnosis, including and not rejecting open thoracotomy. This will remain the crux of good patient care.

Risk-yield-benefit considerations underlie all clinical-surgical management decisions. We will attempt to satisfy the requirements of risk, yield, and benefit in the presentation that follows.

Clinical Material

The records of 50 patients undergoing transaxillary thoracotomy have been analyzed. Four patients had bilateral transaxillary thoracotomies for a total of 54 operations. The relevant data with respect to these procedures is summarized in the Table.

Fourteen transaxillary thoracotomies were performed in 10 patients with spontaneous pneumothorax. Access to the apical blebs was adequate, and it was found that a sufficient pleurodesis or pleurectomy could be accomplished easily through this approach. As to management of the blebs themselves, we found that a very neat method was simply to decrease the cautery coagulation current and apply it around the periphery of the major blebs. The desiccating effect obliterated the majority of the blebs, and the healing process was that of a burn, with scar formation and adherence to the chest wall. Large, localized blebs were treated by stapling and excision. One cannot treat all blebs, regardless of the approach; but since most are located in the apices of the lung, especially in the younger age group, we have found this approach extremely useful.

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Transaxillary Minithoracotomy in 50 Patients

Diagnosis & Indication	No. of Patients	No. of Thoracotomies
Recurrent spontaneous pneumothorax	10	14
Benign cysts and tumors	13	13
Localized primary lung cancer with severe chronic obstructive lung disease	5	5
Unresectable lung cancer; to obtain tissue for complexed BCG vaccine	6	6
Reticulum cell sarcoma of chest wall	1	1
Wedge resection or enucleation of metastatic cancer	7	7
To determine resectability of primary lung cancer[a]	8	8
Total	50	54

[a]Three tumors proved to be resectable; by extending the incision, 1 lobectomy and 2 pneumonectomies were performed.

Certain well-defined circumscribed lesions can occur in the upper mediastinum, upper lobes, or superior segments of the lower lobes. In most cases one has a good idea that these are benign lesions based on the clinical picture and roentgenograms. Hamartomas, granulomas, neurogenic tumors, bronchogenic cysts, and similar lesions fall into this category. We have treated 13 such patients; all proved to have benign lesions easily accessible with the transaxillary approach. Posterior mediastinal lesions could be approached extrapleurally, which was particularly advantageous if pleural adhesions were present.

Complete wedge resections of small, localized, primary lung cancers were performed in 5 patients whose respiratory function precluded any extensive resection. It is these cases which we consider particularly noteworthy. We were impressed with the decreased morbidity and rapid recovery of these patients in the postoperative period compared with the aftermath of the standard posterolateral thoracotomy. There seems no question that this minithoracotomy is accompanied by significantly decreased postoperative pain. This is of obvious benefit, as excessive pain limits adequate respiration.

We used the transaxillary approach in 6 patients with proved unresectable lung cancer in order to obtain a sufficient amount of primary lung cancer tissue for a BCG-complexed cellular vaccine. We cannot comment at this time on the efficacy of this form of immunotherapy but can only point out that this method of obtaining the tissue was expeditious and efficient.

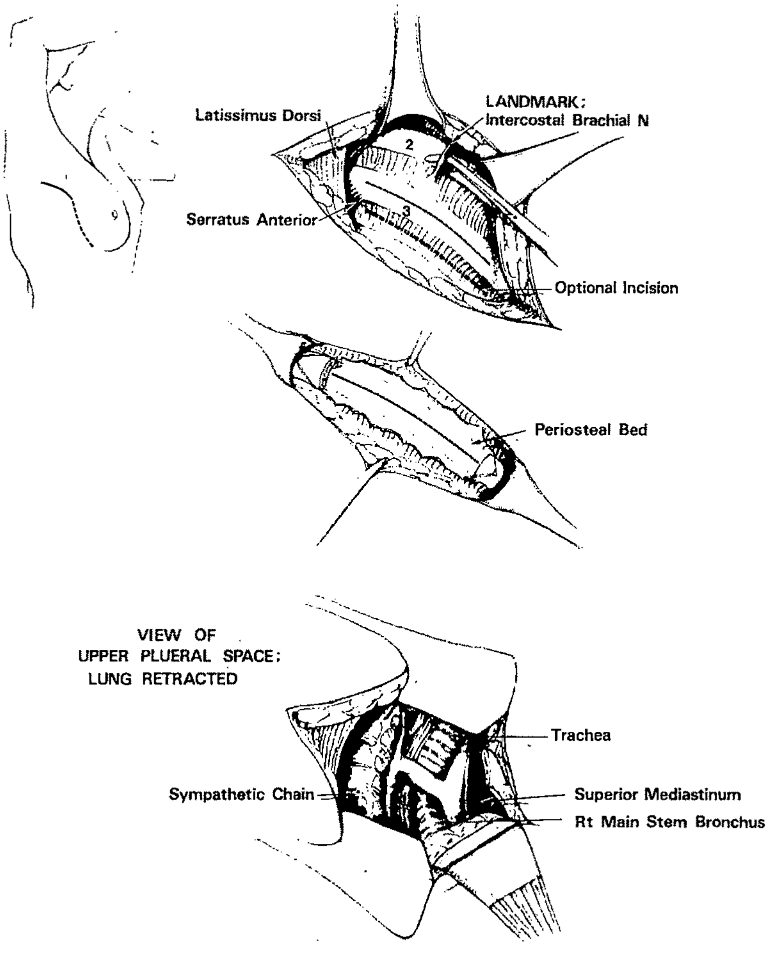
In 7 patients wedge or local excision of metastatic lesions was carried out. Breast cancer was the most common primary lesion. The advantages of the smaller thoracotomy in these patients is apparent.

It seems there always remains a small group of patients in whom lung cancer appears highly likely to be unresectable on clinical grounds but in whom this cannot be proved by lesser means such as mediastinoscopy. The transaxillary approach was chosen to explore operability in 8 such patients. Following the initial exploration and assessment, 3 of the 8 proved to have resectable cancers. By extension of the incision, 2 pneumonectomies and 1 lobectomy were performed without difficulty.

Operative Technique

The patient is placed directly in the lateral position. We find it most convenient to anchor the padded forearm to the crossbar of the anesthetic screen. This keeps the shoulder elevated at a right angle and exposes the axilla very satisfactorily (Figure).

A curvilinear incision is made at the base of the hairline; the incision may have various



Operative technique. (A) Patient position and extension of incision, if required (dotted line). *(B) Incision exposing third rib. (C) Incision into thorax through bed of resected third rib. (D) View of upper right mediastinum with lung retracted.*

shapes and may be extended easily. The draping is done so that if extension is necessary, it can be carried forward anteriorly by curving it in an S shape down and into the crease of the breast in women and to the corresponding position in men. There is very little muscle layer on the chest wall in this location, and the skin and subcutaneous tissue are rapidly cleared down to the chest wall. The latissimus dorsi is retracted posteriorly and the greater pectoral muscle anteriorly. One is usually over the third rib, and the reliable landmark to identify the interspace is the intercostobrachial nerve, which always enters the second intercostal space. One may choose to enter the third interspace or to remove a section of the third rib.

We do not recommend entry through the second interspace or rib bed. We fear that injury or interference with the intercostobrachial nerve could cause intractable postoperative pain.

We prefer to remove a section of the rib. This allows for a window exposure and is much easier to close. The length of the incision or resected rib varies from 15 to 20 cm. In most cases, when the pleura is entered the lung falls free and retracts, and one is able to depress the lung down completely and view the entire mediastinal area from the level of the hilum and above. Assessment of the disease process can then be carried out. The incision is large enough to admit the hand for palpation and to biopsy lymph nodes and masses; and a variety of excisional procedures can be carried out, depending on the circumstances. If after initial assessment one determines that a more extensive procedure such as lobectomy or pneumonectomy is feasible, the incision is simply extended by curving under the breast. This necessitates cutting across the third and fourth rib, but adequate exposure can be obtained by this means and one is not caught in a hopeless situation with a small incision. The postoperative recovery in our 3 patients who had formal resection were no different from what we would have expected with the standard incision.

In most cases the operating time is 30 to 60 minutes. The end result and cosmetic appearance of the scar are gratifying, and the familiar features of excessive postoperative pain and residual intercostal neuralgia are virtually absent. Morbidity is minimal; in our experience it consisted entirely of small pneumothoraces or hemothoraces that caused no complications and cleared rapidly without specific treatment.

Results and Comment

One death, that of a 72-year-old patient, occurred postoperatively among the 50 patients in whom 54 transaxillary thoracotomies were performed. Full shoulder and arm movements returned much more rapidly, since responsible muscles were not disturbed. Healing was rapid; postoperative pain and pulmonary complications were minimal; and hospital stay was shortened, averaging eight days.

With respect to risk-yield-benefit considerations, the risk was that of a normal or less than normal thoracotomy, and the yield in this series was 100%. The benefit considerations are difficult to evaluate accurately; however, we believe that those patients with borderline respiratory insufficiency certainly benefited greatly through the procedure. Patients with spontaneous pneumothoraces were treated rapidly and could be discharged very early. In young women in particular, the benefit of having a scar hidden in the base of the axilla is an enormous psychological advantage.

It takes some practice to become completely familiar with the transaxillary thoracotomy approach. A chest surgeon is prone to become frustrated working through a smaller incision than normal, and those who wish to try this approach should have a little patience and gain some experience before rejecting it outright on the first attempt. The authors are not champions of the small incision, but, like others [2, 3], we believe that small incisions can offer some advantages.

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Discussion

DR. JEAN DESLAURIERS (Quebec City, Que, Canada): I would like to congratulate Drs. Becker and Munro on their presentation and to summarize our experience with a similar approach in the treatment of recurrent and spontaneous pneumothorax. The incision that we use extends from the axilla along the greater pectoral muscle. Through this incision the apex of the lung is pulled out, and in most cases apical bullae are seen and stapled. The apical pleura is then excised as a single sheet. We think that apical pleurectomy alone provides adequate pleural symphysis. By its length and location, this incision causes very little pain. Equally important, no respiratory muscles are divided. These two factors reduce the risks of atelectasis to a minimum. The hospital stay averages four to five days, and most patients are back to work within one month.

In the last 3 years we have performed 110 pleurectomies and have had no recurrences in the 77 patients seen at follow-up. The cosmetic results have been highly satisfactory, especially for women who wish to wear very light clothing.

DR. J. B. SHAMMASH (Springfield, MA): I endorse the transaxillary approach as an effective, limited exposure for a variety of circumstances as outlined by the authors. We have used it in 12 patients with recurrent pneumothorax for apical parietal pleurectomy and for resection and plication of apical cystic areas of the lung. A short horizontal incision below the axillary hairline is made. We do not resect a rib, as the authors do; the pleura is entered through the bed of the fourth rib after the upper border of the rib has been denuded. Pleurectomy from the level of the fourth rib to the cupula of the hemithorax and down to the level of the aortic arch or azygos vein over the mediastinal surface is accomplished without difficulty.

The incision is superior cosmetically, and it preserves the integrity of the shoulder girdle muscles, allowing patients to return to work and to resume their favorite game of tennis or golf within a few weeks, usually free from pain. The incisional pain and late postoperative paresthesia and numbness associated with the standard posterolateral thoracotomy and so disturbing to a young woman, especially in the region of the breast, are avoided. Minimal numbness of the inner aspect of the upper arm in the distribution of the intercostobrachial nerve is the only sequel.

One of our patients who had her menstrual cycle in the early postoperative days complained of a painful swelling near the anterior extremity of the incision due to edema of the axillary tail of the breast. Two patients had had posterolateral thoracotomy on the opposite side a few years earlier for recurrent pneumothorax, and both testified to experiencing far less pain and discomfort from the transaxillary incision.

It is a useful but limited approach. We would not recommend it for extensive pleurectomy or for extensive tailoring of multiple lobes for giant cysts of the lung.

DR. WILLIAM A. COX (Corpus Christi, TX): I commend Drs. Becker and Munro for extending the use of the transaxillary approach. We first started using this approach 7 years ago for resection of the first rib in thoracic outlet compression while I was at Brooke Army Medical Center at San Antonio. We reported these results 3 years ago. We are very satisfied with the transaxillary approach and have continued using it in private practice in Corpus Christi, Texas, with an ongoing series of 68 patients.

We have used the transaxillary approach for dorsal sympathectomy, as the authors mentioned. It gives beautiful exposure of the lower half of the stellate ganglion and of the second through fourth thoracic vertebrae. We have used the approach for operating on causalgia of the upper extremity and for Raynaud's disease. We have also used it for pleural scarification, resection of apical blebs, treatment of recurrent spontaneous pneumothorax, and resection of benign tumors in this area. Transaxillary thoracotomy is also useful for apicolysis in patients with persistent space problems following resection of upper lobes. The incision is less painful than the posterolateral or anterior thoracotomy. It is a functional incision, it divides none of the extracostal muscles, and it gives a very nice cosmetic result.

DR. WILLARD A. FRY (Evanston, IL): I compliment the authors for bringing this incision to our attention. Its most eloquent spokesman in the metropolitan Chicago area is Dr. Robert Jensik, who is well known to this audience. I would like to emphasize the speed of this incision, both in opening and in closing it, and also the lack of postoperative discomfort. At the Evanston Hospital, Northwestern University Medical Center, the axillary thoracotomy is our incision of choice for open biopsy for diffuse lung disease, for elective resection in the poor-risk patient with chronic obstructive lung disease, and for the surgical attack on recurrent spontaneous pneumothorax.

I think that one should not shy away from doing a major resection with this incision; it does not have to be limited to wedge resections. If a double-lumen catheter such as a Carlens or a Robertshaw tube is used, one can push the mediastinum way up and perform pneumonectomies, segmental resections, and lobectomies. One is not limited to a lesser type of resection just because an axillary incision has been chosen.

I would like to make two comments on technique; first, I believe one gains much more versatility if one does not go through the rib bed but rather uses an intercostal incision, because an intercostal incision can be extended much more. Second, if one is really pressed for cosmetic results in a young woman, I believe the anterior submammary thoracotomy may give a better end result. It takes a little longer and there is more postoperative discomfort, but if a main requirement in a diagnostic procedure in a young woman is a good cosmetic result, then I think the submammary incision is superior.

MR. DAVID WATERSTON (London, England): I would like to suggest that the axillary approach is also very applicable for a major thoracotomy in children. The late Sir Denis Browne described this approach for esophageal atresia in the newborn in 1948, and we have used it consistently for the last 25 years.

I do not want to go into too much detail, but I would suggest that especially in children, and particularly girls, a vertical incision high up in the midaxillary line gives a much better cosmetic result. It doesn't go anywhere near the breast, and the scar is completely hidden in the axilla. My residents call it the "bikini incision" because these girls can wear a bikini with no scar in the front or back.

DR. C. FREDERICK KITTLE (Chicago, IL): Patients are demanding more, and with the increasing incidence of thoracotomies for an obvious variety of reasons, more attention should be paid to thoracotomy incisions. Axillary incision has been used at our institution now for about 30 years, and its utility has been well tested in many situations.

We prefer an oblique incision from the posterior axillary line down to the inframammary fold.

An intercostal incision is used which can be extended either posteriorly or anteriorly. We find that about three-fourths of all our thoracotomies for esophageal or mediastinal problems, up to and including sleeve lobectomies and pneumonectomies, can be done adequately through this incision. As Dr. Fry mentioned, generous exposure of the entire hemithorax is obtained if unilateral endobronchial occlusion is used, the lung is atelectatic, and the mediastinum is shifted to the operative side.

DR. BECKER: I thank all the discussants for their confirmatory remarks. I would like to make a few comments with regard to open lung biopsy. I am not sure that this incision has any advantage. A small anterior incision for an open lung biopsy is quite adequate, and especially on the left side, the tip of the lingula pops right through the incision and can be snipped off easily with a stapler. I think it is just as fast and has the same advantages as the transaxillary approach.

I would like to thank Mr. Waterston for his remarks. Under Dr. Dobell's guidance we have been using the Browne incision (vertical incision through the axilla) for several years in Montreal for operating on patent ductus arteriosus. Since I have been in New York I have been doing it extrapleurally, and this approach works very well for the small baby.

I agree with Dr. Kittle that the incision should be carefully planned and that if it follows the rib line, it allows one more flexibility in extending the incision if necessary.

In closing, we think the small incision can be used safely and wisely for many lesions in the chest, mediastinum, and pleural space.

Emergency Open Lung Biopsy

J. M. Nelems, M.D., J. D. Cooper, M.D., R. D. Henderson, M.B.,
T. Peng, M.D., and M. J. Phillips, M.D.

ABSTRACT **Twenty-eight patients underwent open lung biopsy on an emergency basis. The clinical course in each case was deteriorating rapidly, and all were in respiratory failure. The correct diagnosis was established in 96% of the biopsies (27 of the 28 patients). The clinical diagnosis prior to biopsy was in error or incomplete in 15 (55%) of the patients. Specific therapy was lifesaving in 12 of the 28 patients.**

The value of the procedure outweighed the complications. Thrombocytopenia and positive end-expiratory pressure ventilation were not contraindications to biopsy.

Open lung biopsy is being used increasingly to establish the correct diagnosis in patients with acute respiratory failure of uncertain etiology [2, 5]. The precise diagnosis permits specific therapy that may be lifesaving. Our experience with 28 such patients is reviewed in this paper.

Clinical Material

In the past three years 28 patients have undergone emergency open lung biopsy. All were in respiratory failure by blood gas definition (Pa_{O_2} < 50 mm Hg on room air) and were deteriorating due to progressive respiratory failure. Sixteen patients were receiving assisted ventilation at the time of biopsy. Four of the biopsies were performed under local anesthesia in the respiratory care unit in patients receiving assisted ventilation who were judged too ill to be moved to the operating room. These 4 patients were all receiving ventilation with positive end-expiratory pressures of 10 to 30 cm H_2O. Thrombocytopenia was a clinical problem on 4 occasions (see the Table). Platelet transfusions were administered at the time of biopsy.

The site of biopsy was determined by clinical and radiological features. All lung lobes, at different times in this series, were biopsied through limited thoracotomy incisions. The lingula was the most common site of biopsy. A single lobe was biopsied in 21 cases, while two lobes were biopsied in the remaining 7 patients. The lung margins were secured by chromic suture or with the stapling device (GIA autosuture).

In all cases, tissue was submitted for both microbiological and pathological examination. Ziehl-Neelsen and Gram stains were done on touch preparations, and cultures for bacteria, fungus, and tuberculosis were established. Pathological specimens were examined by frozen-section techniques as well as by permanent sections. Hematoxylin and eosin, Gomori's methenamine silver, periodic acid–Schiff, Ziehl-Neelsen, Giemsa, and Gram stains were routinely obtained on the specimens. Electron microscopy was done as indicated.

Serum antibody titers were measured in acute and convalescent stages in patients suspected of having a viral etiology for their disease.

Frozen-section histology and Gram stain results were reported immediately. The results of special stain studies were available 4 hours after tissues were received. Permanent sections were available in 24 hours. In certain selected cases, electron microscopy results were available at 48 hours.

The Table summarizes the clinical aspects and biopsy findings in the 28 patients. Twelve of them had an underlying malignancy.

Results

The biopsy established a correct diagnosis in 27 of the 28 patients (96%), permitting specific therapy to be continued or instituted. The single patient in whom lung biopsy failed to establish the diagnosis subsequently died of bacterial in-

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Clinical Data on the 28 Patients

Patient No., Age, & Sex	Predisposing Factors	Clinical Diagnosis before Biopsy	Biopsy Diagnosis[a]	Treatment	Complications	Result
1,[b] 37, M	Collagen vascular disease	*Pneumocystis carinii*	Cardiovascular disease; organized pneumonia; pulmonary embolus	Ventilatory support; corticosteroid; antibiotic; membrane oxygenator; heparin	None	Died
2, 22, M	Lymphoblastic leukemia in remission	Bacterial infection	Viral pneumonitis	Corticosteroid	None	Recovered
3, 34, M	None	Desquamative interstitial pneumonitis	Disseminated blastomycosis	Amphotericin	None	Recovered
4, 60, M	Adenocarcinoma	Infection	Adenocarcinoma, secondary	Symptomatic measures only	None	Died
5, 19, M	Hodgkin's disease	Infection	Infarcted lung; Hodgkin's disease	Left pneumonectomy; chemotherapy	None	Recovered
6, 71, F	Breast carcinoma	Malignant infiltration	Viral pneumonia	Corticosteroid	None	Recovered
7, 29, F	Malignant thymoma	Radiation pneumonitis	Radiation pneumonitis	Ventilatory support; corticosteroid	None	Died
8, 70, M	None	Interstitial fibrosis; viral pneumonia	Interstitial fibrosis; pulmonary embolus	Ventilatory support; rin; corticosteroid	None	Died
9, 85, F	None	Pneumonia	Bronchopneumonia; pulmonary embolus	Ventilatory support; antibiotic; heparin	None	Died
10, 60, F	Diffuse vasculitis	Collagen vascular disease	Collagenosis pneumonia	Corticosteroid	None	Recovered
11, 53, M	Hairy cell leukemia	Leukemic infiltrate	Viral pneumonia	Corticosteroid	Bleeding—transfusion (2 units)	Recovered
12, 63, M	None	Aspiration pneumonitis	Advanced chronic interstitial fibrosis	Ventilatory support	None	Died
13,[b] 33, M	Embryonal cell carcinoma of testis	Bleomycin lung toxicity	Bleomycin lung toxicity	Ventilatory support; antibiotic; corticosteroid	None	Died
14, 38, M	None	Bacterial pneumonia	Bacterial pneumonia (*Klebsiella*)	Antibiotic	None	Recovered
15, 53, M	Embryonal cell carcinoma of testis	Viral pneumonia; metastatic tumor	Viral pneumonia; metastatic tumor	Ventilatory support; corticosteroid	None	Died
16, 60, M	None	Histoplasmosis of lung	Histoplasmosis	Antibiotic	None	Recovered
17, 22, M	None	Eosinophilic pneumonia	Eosinophilic pneumonia	Ventilatory support; corticosteroid	None	Recovered
18,[b] 60, F	Pancreatitis	Pulmonary embolus; pulmonary edema	Pulmonary embolus; pulmonary edema	Ventilatory support; heparin	Tension pneumothorax; bleeding—transfusion (2 units)	Died
19, 27, F	None	Viral pneumonia	*Pneumocystis carinii*; interstitial fibrosis	Ventilatory support; pentamidine; corticosteroid; antibiotic	Tension pneumothorax; cardiac arrest with resuscitation	Died
20, 33, M	None	Viral pneumonia	Viral pneumonia	Corticosteroid	None	Recovered
21, 51, F	Mixed connective tissue disease	Mixed connective disease	Mixed connective disease	Ventilatory support; antibiotic; corticosteroid	None	Died
22, 21, F	None	Tuberculosis; amniotic fluid embolus	Tuberculosis	Ventilatory support; INH, PAS; rifampin; corticosteroid	Prolonged air leak	Recovered
23, 24, F	Myelogenous leukemia	...	Alveolar proteinosis; tuberculosis	Ventilatory support; membrane oxygenator; corticosteroid: antibiotics (including TB drugs)	Prolonged air leak	Died

Table (Continued)

Patient No., Age, & Sex	Predisposing Factors	Clinical Diagnosis before Biopsy	Biopsy Diagnosis[a]	Treatment	Complications	Result
24,[b] 21, M	None	Viral pneumonia	*Alaria americanis* infestation of lung (lung fluke)	Ventilatory support; membrane oxygenator; corticosteroid; BITIN	None	Died
25, 67, M	Lymphocytic lymphoma	*Pneumocystis carinii*	Viral pneumonia; pulmonary embolus	Corticosteroid; heparin-warfarin	Pneumothorax	Recovered
26, 29, M	Adenocarcinoma colon	Pneumonitis	Adenocarcinoma	Symptomatic measures only	None	Died
27, 60, M	Renal transplantation, immunosuppression	? *Pneumocystis carinii*	*Pneumocystis carinii*	Ventilatory support; pentamidine	None	Died
28, 26, M	Immunoblastic lymphadenitis	Immunoblastic lymphadenitis (former lymph node biopsy)	Compatible with "immunoblastic lymphadenitis" in lung	Ventilatory support; corticosteroid	None	Died

[a] The final diagnosis was the same as the biopsy diagnosis except in Patient 21, who had *Klebsiella* pneumonia.

[b] Thrombocytopenic.

INH = isoniazid; PAS = paraaminosalicylic acid; BITIN = bithional.

fection. Twelve of the 28 patients in this series survived the respiratory illnesses that necessitated the emergency open lung biopsy.

The clinical diagnosis prior to biopsy was incomplete or in error in 15 of these 27 patients (55%). On occasion, only symptomatic measures were undertaken when it became apparent from the clinical course and biopsy diagnosis that death was inevitable.

Complications of this procedure included bleeding in 2 patients treated by transfusion, prolonged air leak from intercostal drains in 2 patients, and tension pneumothorax in 2 patients. One tension pneumothorax led to a cardiac arrest, with subsequent successful resuscitation. The Table documents other results.

Comment

A precise diagnosis was established in 96% of the series by means of open lung biopsy. The complications were not considered excessive in view of the high diagnostic yield.

The working clinical diagnosis prior to biopsy was in error in 55% of the cases. Therapy was altered appropriately when diagnostic information became available. It is clear from the wide spectrum of diagnostic entities encountered that diagnosis may be impossible short of a direct biopsy. For this variety of conditions, therapy varies from the use of high-dose corticosteroids to antibiotics or antimetabolites. What is appropriate therapy in one case may be harmful in another. It is precisely for this reason that at no time did we consider the severity of illness to be a contraindication to open lung biopsy. The more severe the illness, the greater the urgency became to establish the diagnosis.

If necessary, the procedure can be performed at bedside in the intensive care unit using local anesthesia while the patient is receiving assisted ventilation. Patients receiving positive end-expiratory pressure ventilation presented no particular difficulties. Potential hemostatic problems in patients with thrombocytopenia were overcome by the use of platelet transfusions given at the time of biopsy.

Percutaneous biopsy using the aspiration method has been most useful in neoplastic disease [6]. In patients with diffuse lung disease this technique provides scanty cytological material in small specimens; consequently the diagnostic yield is low [6]. The percutaneous technique with cutting needles provides small specimens less suitable for histological assessment [4]. Pneumothorax, bleeding, and air embolism are significant hazards associated with this technique. It is our opinion that percutaneous needle biopsy is contraindicated in patients such as those reported in this series.

Transbronchial biopsy is an effective diagnostic technique, and its use has been described in immunosuppressed patients suspected of having *Pneumocystis carinii* pneumonia and in patients with diffuse pulmonary disease [1, 3, 7]. Our experience with this technique is limited. We believe our evaluation of transbronchial biopsy should be extended in these high-risk and deteriorating patients.

We support the views of those who advocate the value of open lung biopsy [2, 5, 8]. However, we would recommend that the indications for the technique be extended to include those patients in acute respiratory failure who are receiving ventilatory support and those whose clinical course is deteriorating rapidly. This procedure can be employed even in the face of thrombocytopenia and positive end-expiratory pressure.

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Discussion

DR. PHILIP E. BERNATZ (Rochester, MN): I certainly commend the authors for their presentation, particularly for the concept of aggressive early treatment in these very ill patients. It seems fair to emphasize, however, that it is not sufficient simply to perform an open lung biopsy, because only if the physician provides his laboratory colleague with representative tissue in adequate amounts and appropriately preserved can the full benefits of the procedure be realized.

We would disagree a little with the concept of doing the biopsy at bedside, as we rely heavily on the support available in the operating room for these very ill patients. The surgical pathologist is there to help guide us in determining whether we have appropriate tissue. For example, alveolar proteinosis very seldom involves the periphery of the lung, and if you strongly suspect it, you must not complete the procedure without a representative biopsy because this may be your last chance to really benefit the patient.

If we can get at these patients at the outset, we employ a transbronchoscopic technique as described and practiced by Howard Andersen and his colleagues in our institution. Not all my colleagues share this philosophy. These patients must be biopsied prior to the initiation of the shotgun therapy that has commonly been unsuccessful in the past. Our experience with transbronchoscopic biopsy has now grown to 800 cases. Diagnostic tissue is obtained in a high percentage of very ill patients with diffuse disease, but if this method fails, we resort to open lung biopsy.

The data that have been accumulating suggest the wisdom of transbronchoscopic biopsy initially, especially in the acutely ill patients on whom we are focusing. For example, the diagnosis of *Pneumocystis carinii* pneumonia should invariably be made by endoscopic methods. It cannot be denied that experience and appropriate instruments may preclude this technique being standard everywhere, but the experts in this audience might give it a careful look.

DR. LAWRENCE L. MICHAELIS (Chicago, IL): At the National Institutes of Health during the last three years we have performed urgent open lung biopsy for diffuse pulmonary infiltrates in 40 patients whose immunological status was compromised. All were hypoxemic, and the majority were thrombocytopenic or leukopenic. Our diagnostic results were similar to those reported by Dr. Nelems, and in our series of patients there has been only 1 complication: a wound separation four weeks postoperatively in a child on high-dose corticosteroids.

I would like to reinforce one point that Dr. Nelems has made: a sizable number of these very ill patients have a curable infection, but it is curable only if an early and accurate diagnosis is made and if inappropriate therapy is avoided. Lung biopsy provides an accurate diagnosis, and as has been pointed out, more than half of the patients have had an incorrect preoperative clinical diagnosis.

As chemotherapy for malignant disease and organ transplantation becomes increasingly effective, the number of patients with these bizarre, atypical, diffuse pulmonary inflammatory processes is going to increase. I think it will behoove us, as thoracic surgeons, to become better acquainted with these diseases because we are going to be more and more involved in the care of these patients.

We are convinced that urgent open lung biopsy in these critically ill patients is the safest procedure; not only is adequate tissue obtained for performance of diagnostic studies, but the risks of closed biopsy techniques, which are magnified in these already compromised patients, are avoided.

DR. NELEMS: I am grateful to the discussants for agreeing with the main thrust of our paper. Dr. Michaelis' patients were all individuals who had had immunological suppression, and indeed, in his patients one would expect the high incidence of opportunistic infection that they found. It is pleasing to hear him agree that these infective illnesses are highly treatable.

Dr. Bernatz and his colleagues from the Mayo Clinic have documented a wide experience in the use of transbronchial biopsy. I think it has a place in the management of these patients. However, we have not evaluated this to our complete satisfaction. We have considered that time is of the essence, and we have been reluctant to rely on the small piece of tissue available at transbronchial biopsy because we subject the specimen to many stains and an extensive diagnostic protocol. Therefore we have aimed at taking a large chunk of tissue early. The place for transbronchoscopic biopsy may be in the management of those less emergent but yet somewhat urgent cases for which one still has 12 to 24 hours in which to evaluate the patient's status.

I agree with Dr. Bernatz that the biopsy ideally is not performed at the bedside. Most of our patients, and certainly most of those on ventilators, have had it done in the operating room. However, in 4 instances we did the procedure at the bedside because we considered the patients too critically ill to be detached from their respirator and ventilated by bag-mask on their way to the operating room.

Mediastinopleuroscopy: A New Approach to the Diagnosis of Intrathoracic Diseases

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ABSTRACT **With the advent of modern therapy, it has become essential to obtain a tissue diagnosis in all cases of pulmonary and mediastinal disease. Since it is often necessary to resort to thoracotomy as a final step in making such a diagnosis, we have sought a procedure that is simpler while capable of providing the same information.**

Through a standard cervical mediastinoscopy incision, the mediastinum is first explored; if the diagnosis is not obtained, the mediastinal pleura is digitally opened and lung or pleural biopsies are taken. In the course of 1,100 mediastinoscopies since 1969, 275 pleuroscopies have been done. We were able to obtain a tissue diagnosis in 102 (78%) of 131 patients with bronchogenic carcinoma, in 92 (91%) of 102 with benign pulmonary disease, and in all 20 (100%) with pleural disease.

With the advent of modern therapy for pulmonary diseases, it has become more and more useful, desirable, and indeed often necessary to obtain histological confirmation of a radiological, cytological, or bacteriological diagnosis. As a final step in the making of such a diagnosis, the surgeon often has to resort to a diagnostic thoracotomy. Starting in 1959 with Carlens' description [5] of a cervical approach to the mediastinum, a variety of methods have been devised in an attempt to obtain tissue for microscopical study or to determine the operability of bronchogenic carcinoma [1–24]. All these methods have one common denominator: to avoid an unnecessary thoracotomy.

In our experience, mediastinopleuroscopy has become a logical extension of Carlens' cervical mediastinoscopy. By adding pleural exploration to mediastinal evaluation, we have been able to complete the investigation of patients with pulmonary disease with a maximum of safety and minimal morbidity.

Technique

Under general anesthesia, we first perform a standard cervical mediastinoscopy according to Carlens' technique [5]. A full mediastinal exploration includes biopsies from the paratracheal, tracheobronchial, and carinal lymph nodes. If the histological diagnosis is not established by these biopsies, the pleural space is entered by digital perforation of the mediastinal pleura. On the right side the pleural opening is made just behind the innominate artery, while on the left the dissection and opening are made between the left subclavian and common carotid arteries (Fig 1). Dissection in front of the common carotid artery is difficult and can produce laceration of the internal mammary artery or one of its branches.

The mediastinoscope is then introduced in the pleural space, and after exploration has been carried out, biopsies are taken (Fig 2). In the case of a diffuse pulmonary infiltrate, the lung can easily be pulled out through the suprasternal incision for regular wedge biopsy (Fig 3). If the lesion is more localized, we prefer to do a needle biopsy. The hole made in the lung is immediately cauterized to ensure hemostasis as well as to prevent dissemination of the underlying pathological process. For pleural biopsies we use the conventional mediastinoscopy biopsy forceps. In all cases an adequate amount of tissue can be provided to the pathologist for microscopical study.

After lung biopsies have been taken, a chest tube is left in the pleural space and brought out through the cervical incision. This tube can usually be removed within 24 hours.

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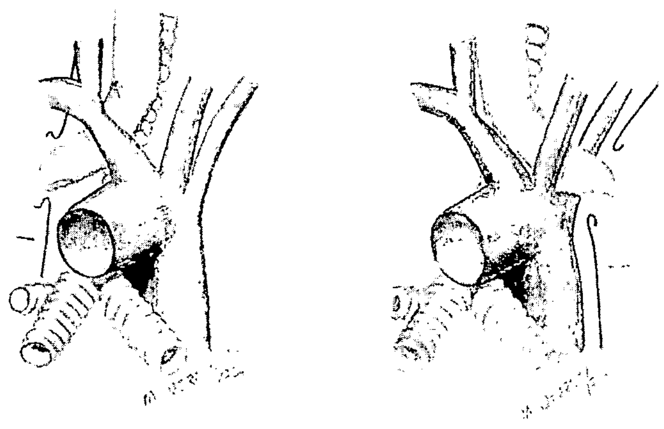

Fig 1. Digital perforation of mediastinal pleura (right and left).

Clinical Material and Results

Between 1969 and 1975, a total of 1,100 patients underwent mediastinoscopy for mediastinal, pulmonary, or pleural lesions. Of these, 275 had a mediastinopleuroscopy. This group of 275 patients was divided in three subgroups, the final diagnosis being bronchogenic carcinoma in 153, benign pulmonary disease in 102, and pleural disease in 20.

In 131 patients with bronchogenic carcinoma the diagnosis was unknown even after mediastinal biopsies, and the object of the procedure was precisely to define the diagnosis before resection. In 102 patients, or 78% of these 131, we were able to confirm histologically the cell type of the malignant tumor (Table 1). In 22 patients the procedure was done to complete the assessment of operability of the carcinoma.

In benign pulmonary disease we obtained a diagnostic accuracy of 91% (92 of 102 patients). A review of the diagnoses obtained can be seen in Table 2. We found it particularly useful in patients who had a localized mass when first seen that suggested bronchogenic carcinoma and in whom we were ready to recommend a pulmonary resection.

All pleural diseases (Table 3) that we investigated were characterized by a pleural effusion

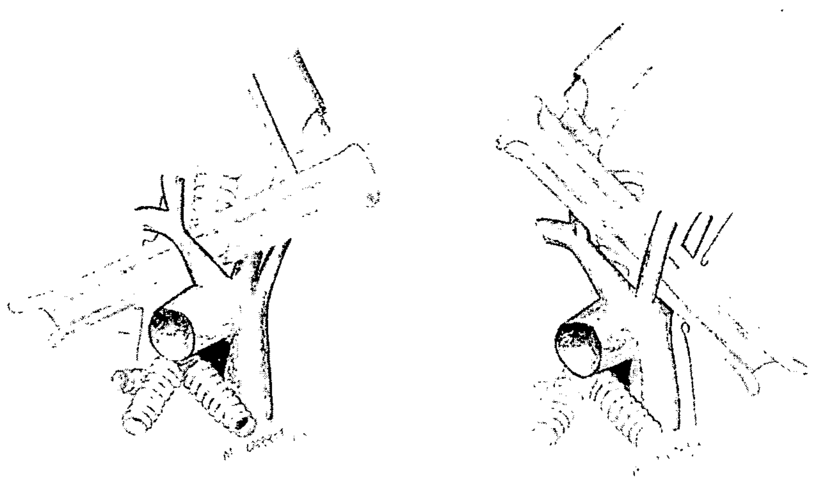

Fig 2. Mediastinoscope in the pleural space (right and left).

Fig 3. Portion of lung as seen through the cervical incision.

for which we had no diagnosis even after mediastinoscopy. In these 20 patients a preoperative clinical diagnosis of malignant effusion had been entertained. The preoperative diagnosis proved to be correct in only 10.

Limitations and Complications

Our exploration of the pleural cavity is limited by the anatomy as well as by our rigid instrumentation. The right middle lobe and the lingula are located too far anterior to be seen, while the basal segments of the lower lobes are seen but are difficult to obtain biopsies from. Both upper lobes and the superior segments of the lower lobes are readily accessible to biopsy. Another limitation to this procedure is an obliterated pleural space. This prevents safe manipulation and biopsy; fortunately, very few patients have this difficulty.

The problem of left upper lobe and left hilar tumors, with their lymphatic drainage, is partially solved. A left pleuroscopy allows biopsy of lymph nodes in the preaortic region and anterior to the common carotid artery. Subaortic nodes are not seen, however, and as advocated by Pearson and colleagues [16], we prefer a left anterior mediastinotomy for exploration of that nodal area.

We have encountered very few complications by adding a pleuroscopy to mediastinoscopy. One patient needed a sternotomy for bleeding originating from the internal mammary artery. This was our first case, and the left pleural exploration had been done anterior to the common carotid artery. Since that time the dissection has been carried out between the carotid and the

Table 1. Diagnoses by Mediastinopleuroscopy in 275 Patients

Disease	No. of Patients	Histological Diagnoses Number	Histological Diagnoses Percent
Pulmonary (malignant)	131	102	78
Pulmonary (benign)	102	92	91
Pleural	20	20	100

Table 2. Diagnoses by Mediastinopleuroscopy in 102 Patients with Benign Pulmonary Disease

Diagnosis	No. of Patients
Pulmonary sarcoidosis	30
Pneumoconiosis	15
Pulmonary tuberculosis	12
Pulmonary fibrosis	9
Interstitial pneumonitis	6
Mycosis	3
Miscellaneous	17

Table 3. Diagnoses by Mediastinopleuroscopy in 20 Patients with Pleural Disease

Diagnosis	No. of Patients
Inflammatory disease (nonspecific pleuritis)	10
Metastatic carcinoma	8
Mesothelioma	2

subclavian arteries. Fifteen patients developed pneumothorax, but only 2 needed chest tube drainage.

Comment

Following Daniels' description of scalene node biopsy [6], Carlens was the first to introduce the concept of mediastinal exploration through a cervical approach [5]. His method has been and still is widely recognized in North America as an important step in the preoperative evaluation of patients with bronchogenic carcinoma [2, 7, 9, 14–16, 19, 21]. Furthermore, it is frequently performed in order to make a diagnosis in benign pulmonary disease [8, 18, 20, 24]. Stemmer and associates [22, 23] and McNeill and Chamberlain [13] have also described a parasternal approach to the mediastinum and pleural space.

In our experience, mediastinopleuroscopy has proved to be a very useful procedure; most of the time it has oriented the patient's treatment. In the first place, we can evaluate the hilar and mediastinal lymphatic spread of lung carcinoma by complete mediastinal exploration through a standard mediastinoscopy. If the diagnosis is still unknown, particularly in benign disease, we have the option of opening the mediastinal pleura for direct lung biopsy. This provides us with a tissue diagnosis in most cases. As a result, the number of diagnostic thoracotomies has dropped considerably, demonstrating one of the major advantages of this procedure. We believe that the low morbidity associated with this exploration makes it safer for the patient than a formal thoracotomy. Equally important, the discomfort is minimal, being no worse than that occurring after a routine mediastinoscopy.

We would like to point out, however, that by this procedure we do not pretend to solve all pulmonary diagnostic problems. Mediastinopleuroscopy is an attractive alternative, but it does not replace the other diagnostic methods such as diagnostic minithoracotomy or other less invasive techniques.

In summary, we have presented a method for simultaneous exploration of the mediastinum, pleural space, and pulmonary parenchyma that can be used as a last step in establishing a tissue diagnosis before resection or medical treatment is recommended. Its safety and ease of performance, as well as the low morbidity, should make this procedure valuable to all chest surgeons.

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Discussion

DR. RALPH J. LEWIS (Piscataway, NJ): I commend the authors for a most interesting presentation. During the last five years we have utilized this procedure on occasion with beneficial results. It was limited, however, to that group of patients considered to have unresectable disease but in whom we wanted confirmatory tissue without having to do a major thoracotomy. Because of very limited exposure with this procedure, extreme difficulty in entering the left chest due to the anatomical position of the aorta, and finally the inability to evaluate the lower thorax and its contents adequately for metastatic involvement, we have turned to another procedure.

In selected patients the cervical area and involved chest are draped in continuity, and mediastinoscopy is carried out in routine fashion. I must emphasize, we select our patients very carefully for this procedure. If malignant tissue cannot be obtained from the mediastinum, then an incision approximately 4 cm in length is made through the chest wall into the thoracic cavity using the same set of instruments. The mediastinoscope is inserted into the thoracic cavity, and excellent visualization of the visceral and parietal pleura is obtained. Intrathoracic structures can be readily evaluated. Very generous biopsies are easily obtained, allowing frozen sections to be done. In many instances we have been able to avoid a diagnostic thoracotomy. We have had no morbidity or mortality utilizing this procedure, and it added very little time to the mediastinoscopy.

DR. ROBERT GINSBERG (Toronto, Ont, Canada): I too would like to congratulate Dr. Deslauriers for a beautifully presented article. I think this technique is most interesting in the diagnosis of benign pulmonary nodules. We have tended to use needle aspiration biopsy, which is very effective in diagnosing malignant disease. With benign tumors, however—as was the case with 15 of Dr. Deslauriers' patients—needle aspiration has not proved the diagnosis in most cases. This new method should be very valuable since a core biopsy can be taken under direct vision and the diagnosis of a granuloma or similar process can be made, thus avoiding thoracotomy.

DR. CHARLES P. BAILEY (New York, NY): I wish to raise a question about the use of the radial artery for blood pressure monitoring in such a procedure when it probably is not reasonably necessary. We are aware that anatomically the ulnar artery contributes to the blood supply of the hand in only 97% of patients. There is a risk of producing ischemia of the hand when the radial artery is used for monitoring. If it can be demonstrated that blood flows both ways when the radial artery is punctured, then the procedure should be safe.

DR. DESLAURIERS: We first began routinely using a radial artery pressure line for every mediastinoscopy after 1 patient never woke up following the procedure. We then found that cases of left hemiparesis had been reported, presumably because of innominate artery compression. We therefore thought that we should have a way of monitoring these patients, especially during a pleuroscopy. Radial artery monitoring is done in our institution by the anesthesiologists, and they have reported their series of more than 1,500 cases without one complication (American Society of Anesthesiology, Atlanta, October 1970).

I agree with Dr. Lewis that there are other ways of obtaining a diagnosis, especially when the lesions are located in the lower lobes; we also do a minithoracotomy or other procedure to obtain a tissue diagnosis in such cases.

Dr. Ginsberg's comment brings up one point that is important in this paper. It is that pleuroscopy will provide enough tissue for a histological diagnosis in most cases.

Carcinoid Tumors of the Lung

Nsidinanya Okike, M.D., Philip E. Bernatz, M.D.,
and Lewis B. Woolner, M.D.

ABSTRACT **Resection of typical bronchial carcinoid was carried out in 203 patients. The average age was 48 years, and the sex distribution was approximately equal. Bronchoscopy was the most definitive diagnostic procedure, even though 15% of the tumors were located in the segmental bronchus or beyond. Conservative resection including local removal of the lesion was the treatment of choice, but distal suppuration and location of the tumor necessitated pneumonectomy in 54 (27%) of the patients. The incidence of metastasis was 5% (11 patients), and the overall hospital mortality was 3%. Of patients who qualified for follow-up, 94% survived 5 years, and of those who were asymptomatic preoperatively, 98% survived 5 years. The 10- and 25-year survival rates for the group as a whole were 87 and 66%, respectively.**

Bronchial carcinoid was first recognized by Laennec [12] in 1831 and was described by Müller [13] in 1882, but it was not finally established as a clinical and pathological entity until Kramer [11] wrote of it in 1930. Arrigoni and colleagues [1] in 1972 described a series of patients with atypical carcinoids selected on the basis of diagnostic histopathological criteria and the more aggressive behavior of the tumor. Not all authors [14] agree on the aggressive nature ascribed to carcinoids with atypical morphological features and would justifiably point out the occasional difficulty in distinguishing microscopically between a bronchial carcinoid and undifferentiated carcinoma of the small cell type.

Definitions

Typical bronchial carcinoid tumors (Fig 1) are characterized by grouping of cells in nests, ribbonlike structures, or broad sheets, giving an alveolar or glandular appearance. There is an orderly arrangement of cells with stromal tissue of various thickness and vascularity separated by septa. The small polyhedral cells contain small round or oval nuclei and slightly granular acidophilic cytoplasm. Pleomorphism, increased mitotic activity, and disorganization of architecture are absent.

Atypical carcinoid (Figs 2, 3) is characterized by one or a combination of histological features such as increased cellularity with pleomorphism and irregularity of nuclei, hyperchromatism, focal necrosis, and an abnormal nuclei-cytoplasmic ratio. Increased mitotic activity, even in the presence of a recognizable carcinoid pattern, is generally a feature of atypical bronchial carcinoids. This is true whether a recognizable carcinoid pattern is maintained or if a spindling of tumor cells is noted. In our series, atypical carcinoid tumors were characterized by more active biological behavior together with an increased incidence of metastasis and a less favorable prognosis. Metastasis developed in 19 (66%) of the 29 patients who had histologically atypical carcinoids as compared with 11 (5.4%) of the 203 patients who had histologically typical carcinoids. The 5-year survival rate for patients with atypical carcinoid was 57%. The Mayo Clinic experience with atypical carcinoid was reviewed by Arrigoni and associates [1] in 1972. The present study concentrates primarily on the typical bronchial carcinoid tumors.

Materials and Methods

At the Mayo Clinic from 1935 until December, 1973, 246 patients received treatment for bronchial carcinoid. Fourteen of the 246 patients were treated solely by endoscopic techniques in earlier years, with limited tissue available for histological review, so these patients were excluded from the study. Surgical resection was carried out on 232 patients, and specimens from these operations were available for study. Of these, 29 tumors were atypical bronchial car-

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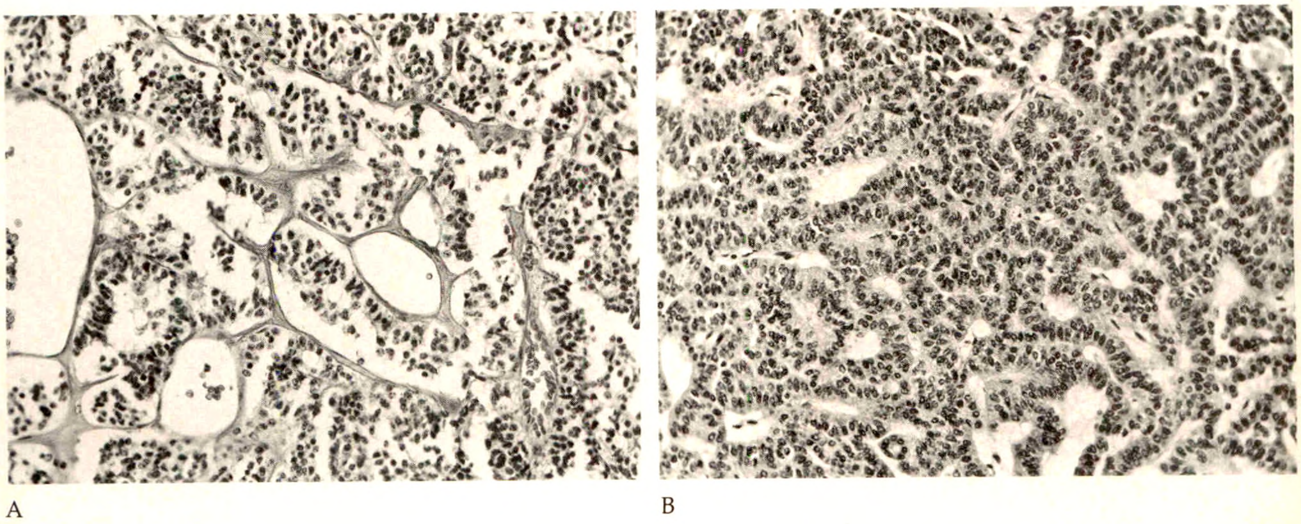


Fig 1. Typical bronchial carcinoid. (A) Carcinoid tumor composed of small cells in cords and nests with a slight glandular pattern. (B) Another example showing slightly larger cells with a prominent glandular and ribbonlike pattern. (Both H&E; original magnification ×200.)

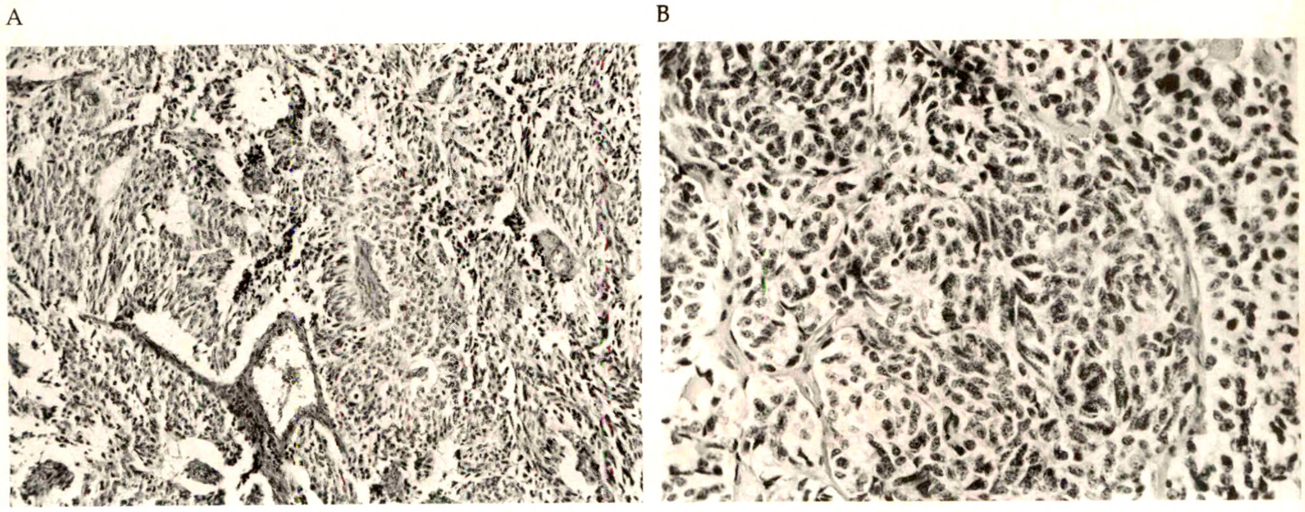
cinoids. The clinical and pathological findings as well as follow-up results on the atypical tumors have been previously published [1]. The present study concerns the 203 typical carcinoids, which comprise 87% of the total. Follow-up information was based on repeat examinations of the patient and on communications with the patient, his physician, or both.

Clinical Observations

Of the 203 patients with typical bronchial carcinoid, 108 were men and 95 were women. Their ages ranged from 15 to 73 years, with the mean age being 47.9 years.

Most patients had symptoms secondary to bronchial obstruction when first seen: chronic cough (61.5%), hemoptysis (42%), recurrent pneumonitis (42%), and fever. Other symptoms

Fig 2. Atypical bronchial carcinoid. (A) Low-power view of atypical carcinoid tumor showing small spindled cells in somewhat organoid pattern. Occasional mitotic figures are seen. (H&E; original magnification ×100.) (B) Higher power view of atypical carcinoid showing nuclear enlargement and hyperchromatism. (H&E; original magnification ×200.)



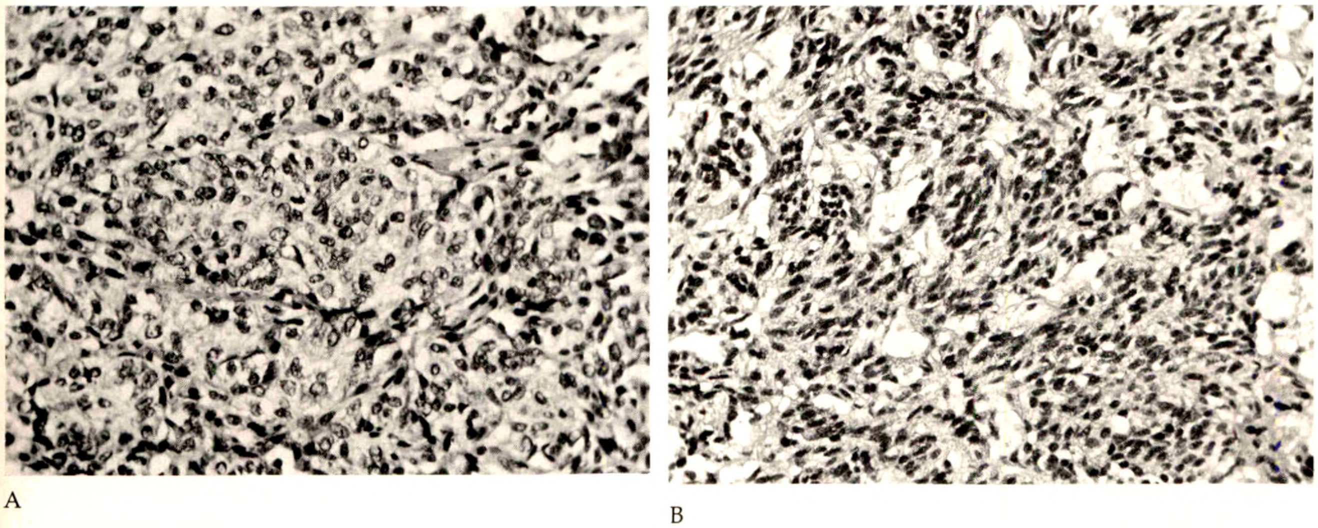


Fig 3. Atypical bronchial carcinoid. (A) Carcinoid tumor showing considerable variation in size and shape of cells with mitotic activity. (H&E; original magnification ×245.) (B) Highly atypical example showing spindle cells, hyperchromatism, and prominent mitotic activity. (H&E; original magnification ×200.)

in order of relative occurrence were chest pain, malaise, dyspnea, wheezing, loss of weight, and diarrhea. Of the 203 patients, 52 had no symptoms referable to the carcinoid. Three patients presented a symptom complex that was characteristic of the carcinoid syndrome.

Roentgenological Features

The chest roentgenogram revealed a central mass alone in 69 patients and a peripheral lesion alone in 35 patients (Table 1). Peripheral implies a tumor in the segmental bronchus or beyond. In 30 patients, the central mass was associated with obstructive pneumonitis. In 44 patients, loss of lung volume without evidence of tumor was the incriminating roentgenographic feature.

Although the tumors were as large as 8.0 cm in diameter, many were not evident on routine roentgenograms of the chest, and secondary phenomena such as obstructive pneumonitis and hemoptysis provided indications for bronchoscopy. This examination was the most definitive diagnostic procedure.

Bronchoscopy

Of the 140 patients who had bronchoscopy, 86% had diagnostic tissue obtained by biopsy, although biopsy was not attempted in some patients because endoscopic findings were characteristic of carcinoid, and excessive bleeding may ensue with biopsy of these tumors. Bronchoscopy was negative in 16 patients, most of whom had peripheral lesions. Because carcinoids may be covered with intact mucous membrane, the results of biopsy may be misleading.

Cytological Findings

Of 133 patients who had cytological examination of sputum or bronchial secretions, 5 had malignant cells. The small cells found in the secretions suggested that the lesion was a bronchogenic carcinoma of small cell type or a lymphosar-

Table 1. Roentgenographic Findings and Average Size of Lesions in 203 Patients with Typical Bronchial Carcinoid

Finding	No. of Patients	Average Lesion Size (mm)
Abnormal		
Central mass	69	24.8
Peripheral mass	35	23.8
Mass and distal pneumonitis	30	23.3
Loss of lung volume (pneumonitis & atelectasis)	44	20.8
Bronchiectasis	4	19.0
Normal	21	11.7

coma. Because there is very little shedding of tumor cells, cytological techniques are not very helpful in preoperative investigations of bronchial carcinoids and obviously can be misleading as to the character of the tumor.

Gross Findings

One hundred twenty-six carcinoid tumors were located in the right lung and 91 in the left lung (Table 2). Ten patients had lesions involving two ipsilateral lobes. Two patients had involvement of the left main bronchus and left upper lobe by carcinoid tumor, and 1 patient had involvement of the right main and right intermediate bronchi as well as the right upper lobe.

The lower lobe bronchi were the predominant locations for the typical bronchial carcinoid (see Table 2). Fifty tumors were located in the right lower lobe, and 44 lesions were located in the left lower lobe. A total of 59 (27%) of the tumors were located in the upper lobe bronchi, 28 of which were in the left upper lobe and 31 in the right upper lobe.

The sizes of the typical carcinoid tumors varied between 0.6 and 6.5 cm, measured across the greatest diameter; the average size was 2.2 cm.

Of the 168 central carcinoid tumors, 50 were pedunculated. Sessile typical carcinoid tumors were found in 118 patients. Exobronchial extension of central lesions was documented in 21 patients. The 35 peripheral carcinoid tumors were generally well circumscribed, with only 1 lesion involving the pleura.

Eleven patients (5.4%) with histologically typical bronchial carcinoid had regional nodal metastases.

Treatment and Complications

Therapeutic modalities ranging from local endoscopic excision to pneumonectomy were employed (Table 3). Between 1935 and 1948, endoscopic removal with fulguration was the initial treatment in 9 patients. All 9 patients eventually had pulmonary resections—pneumonectomy in 8 and lobectomy in 1; the operation was done as long as 12 years after the endoscopic treatment. Local recurrence or parenchymal suppuration secondary to bronchial obstruction was the reason for reoperation in these patients.

Sleeve resection of a portion of bronchus alone was the definitive form of treatment in 4 patients with polypoid endobronchial lesions, and in 5 other patients sleeve resection and lobectomy were performed. Segmental resection was done in 9 patients who had exclusively peripheral lesions without pleural involvement.

Of the 54 patients who underwent pneumonectomy, 7 developed empyema, 1 developed a bronchopleural fistula, and 4 died postoperatively. The most common indication for pneumonectomy was suppuration distal to the obstructive tumor. Lobectomy (including bilobectomy) was carried out in 131 patients.

Table 2. Primary Sites of Typical Bronchial Carcinoids in 203 Patients

Carcinoid Location	Central	Peripheral	Total[a]
Right	104	22	126
Main bronchus	7	0	7
Intermediate bronchus	11	0	11
Upper lobe	27	4	31
Middle lobe	20	7	27
Lower lobe	39	11	50
Left	79	12	91
Main bronchus	17	0	17
Upper lobe	25	3	28
Lingula	2	0	2
Lower lobe	35	9	44

[a] Twelve patients had two ipsilateral sites involved, and 1 had disease at three sites.

Table 3. Types of Treatment for Typical Bronchial Carcinoid in 203 Patients

Treatment	No. of Patients
Pneumonectomy	54
Lobectomy including bilobectomy	131
Segmental resection	9
Sleeve resection & lobectomy	5
Sleeve resection alone	4
Total	203

Postoperatively 3 patients had empyema and cardiac dysrhythmia, 1 had bronchial stricture, and 1 died.

The overall mortality rate in the immediate postoperative period was 3% (6 patients). Two patients died from respiratory insufficiency, 1 died from hemorrhage, 1 from low cardiac output, and 1 from renal failure. The cause of death in 1 patient who underwent pneumonectomy could not be determined.

Follow-up

Follow-up information was available for 190 of the 197 patients who survived the operation. Table 4 summarizes the results in 169 patients who lived 5 years or more. The overall 5-year survival rate was 94%.

If regional nodes were involved with metastasis, 71% of these patients were alive at 5 years. Of special interest is the fact that 96% of the 138 patients who had central lesions survived 5 years as compared with 87% of the 31 patients who had peripheral lesions. Of the 52 patients free of symptoms at the time of diagnosis, 98% survived 5 years. The size of the tumor did not seem to influence the survival rate.

Of the 54 patients treated by pneumonectomy, 88% were alive after 5 years, whereas 96% of the 131 treated by lobectomy, including bilobectomy, were alive after the same period. Seven of the 8 patients who survived segmental resection were alive after 5 years, whereas 6 of the 9 patients treated with sleeve resection were alive after 5 years.

In only 4 patients did distant metastases become evident within 8 years of their curative resection. These metastatic lesions were located in the liver (2 patients), right femoral area (1 patient), and anterior abdominal wall (1 patient). One of these patients had had carcinoid syndrome before operation. This patient died 8 years after left lower lobectomy, and at postmortem examination metastases to the liver, spleen, and adrenal glands were documented.

Comment

The term *bronchial adenoma* has been used since 1930 [11] to designate a group of tumors characterized generally by slow growth, intrabronchial location, and an origin from the mucous glands of the bronchus. The efforts by Hamperl [8] in 1937 popularized the division of this group of tumors into bronchial carcinoid, cylindroma, and mucoepidermoid tumors. These three divisions are now recognized as distinct pathological entities because each has different histological features and a different biological course; hence they should not be grouped together under such a designation as bronchial adenoma. Rare examples of true adenomas of bronchial gland origin have been described.

The histogenesis of bronchial carcinoid and its possible relationship to small cell carcinoma have been of much interest. In 1967 Gmelich, Bensch, and Liebow [7], using electron micros-

Table 4. Late Postoperative Results in 169 Patients with Typical Bronchial Carcinoid

		5-Yr Survival			10-Yr Survival			20-Yr Survival			25-Yr Survival	
	Total	No.	%	Total	No.	%	Total	No.	%	Total	No.	%
Typical carcinoid patients as a whole	169	159	94	136	118	87	80	61	76	47	31	66
Patients with:												
Central lesions	138	132	96	113	99	88	70	54	77	42	28	67
Peripheral lesions	31	27	87	23	19	83	10	7	70	5	3	60

copy, demonstrated the presence of Kulchitsky's cells (argentaffine cells) within bronchial mucosal glands. Bensch and colleagues [3, 4] have shown that cells of small cell carcinoma and of bronchial carcinoid contain neurosecretory granules, and they postulated that the cells arose from a neurosecretory type of cell (Kulchitsky's cells). On the basis of *A*mine content, amine *P*recursor *U*ptake, and amino acid *D*ecarboxylation within the carcinoid tumors and small cell carcinomas, Pearse [14] has recently grouped them into the APUD cell series. The APUD cells can produce amine and polypeptide hormones commonly associated with carcinoid [5, 6, 10, 17] and Cushing's syndrome [2, 9, 16], respectively.

Although most small cell carcinomas and bronchial carcinoids are readily identified by the use of light microscopy, a few transition forms (atypical or malignant carcinoids) are seen. Such tumors present atypical histological patterns and have a more aggressive growth pattern, with metastasis in 66% of tumors as compared with 5.4% of typical carcinoids [1].

Treatment of bronchial carcinoid should be as conservative as possible. In the past, chronic bronchial obstruction with distal suppuration has necessitated rather extensive resections. More recent surgical treatment has consisted predominantly of lobectomy, segmental resection, or local tumor removal with or without a sleeve of bronchus. Endoscopic treatment (cautery) of a predominantly endobronchial tumor in a poor-risk patient may be a reasonable choice on rare occasions. Because many of the tumors are polypoid and possibly could obstruct major bronchi during the course of surgical maneuvers, a double-lumen tube for conduction of anesthesia is appropriate. The surgeon could then be confident that a portion or all of a polypoid tumor would not be lost into the opposite lower lung. Metastatic carcinoid tumor should be treated vigorously, because prolonged survival can be achieved. Other modes of therapy have not proved helpful enough to displace energetic resection of recurrent disease, although some benefit from irradiation and chemotherapy has been observed by us and others in the management of more disseminated bronchial carcinoids [15].

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Discussion

DR. JOSEPH S. MC LAUGHLIN (Baltimore, MD): I congratulate Dr. Okike and his associates on their very fine clinical study and presentation. When I was invited to discuss this study, my associate, Dr. Attar, and I looked back through our experience at the University of Maryland Hospital. We found that we had had some 29 patients with bronchial carcinoids during the past several years, 38% of whom showed some evidence of malignant disease—local invasiveness, positive lymph nodes, and in a few, metastasis to distant areas.

The differentiation between typical and atypical carcinoid is an important one to make, since in the former group our survival rate—and that of Dr. Okike—is above 95% for 5 years. An atypical carcinoid tumor is somewhat similar to oat cell carcinoma in appearance but is actually quite different when viewed under an electron microscope. Patients with atypical carcinoid have less than a 50% chance of surviving 5 years and in some cases even less. But even with typical carcinoids there can be surprises. We had a patient with a typical carcinoid tumor. Approximately a year following the operative procedure the patient developed carcinoid syndrome, and approximately 2 years after that the patient died from widespread metastases.

In view of the problem with typical and atypical carcinoids, I would ask Dr. Okike two questions: first, how reliable is frozen-section diagnosis in differentiating between these two tumors? Second, how does one treat typical as opposed to atypical carcinoids?

DR. L. PENFIELD FABER (Chicago, IL): We support the authors on their premise that conservative resection is the treatment of choice for carcinoid adenoma. During the past 19 years 39 patients have undergone resection for bronchial carcinoid at Presbyterian-St. Luke's Hospital in Chicago. Efforts were made to accomplish conservative resections and to carry out procedures that were alternatives to lobectomy and pneumonectomy whenever feasible. The procedures done were bronchotomy excision of the adenoma in 4 patients, segmentectomy in 11, sleeve resection in 12, lobectomy in 10, and pneumonectomy in only 2 patients. The majority of operations, 70%, were bronchotomy excision, segmentectomy, or sleeve resection. Occasionally one may encounter a patient with mediastinal lymph node disease or a large lesion in which conservative resection is not feasible. However, in the majority of instances a limited resection is appropriate. Only 1 patient in this series has had recurrence and dissemination of the carcinoid tumor.

Sleeve resections were done in 12 patients in our series. They were of the main bronchus in 4, the upper lobes in 3, the middle lobe in 2, a lower lobe in 1, and a superior segment of the lower lobe in 2 patients.

Bronchoplastic and conservative resectional procedures can be done safely with a low recurrence rate. One must remember that a sleeve resection is an alternative to pneumonectomy, and we would urge surgeons to make every attempt to salvage lung tissue when dealing with this type of tumor.

I would like to ask Dr. Okike if reassessment of the 25% of the patients who underwent pneumonectomy in his series would indicate that possibly a more conservative or sleeve type of procedure could have been done.

DR. PAUL A. KIRSCHNER (New York, NY): I support the authors' contention that recurrent lymph node metastases should be resected whenever possible. A recent patient of ours originally had had a right pneumonectomy in 1943 at the age of 18; he was treated then by Drs. Harold Neuhof and Arthur Aufses. The specimen showed a typical carcinoid with a large extrabronchial component, and lymph node metastasis and perineural lymphatic invasion were present.

He appeared 32 years later, in 1975, with superior vena cava obstruction syndrome. Venography showed an exquisitely localized pressure defect of the proximal vena cava. Venous pressure in the arms was 53 cm H_2O. There was no clinical evidence of carcinoid syndrome.

The metastatic nodule producing the vena cava obstruction, which also showed a typical carcinoid pattern, was removed by median sternotomy. It had compressed but had not invaded the caval wall.

Postoperatively the blood serotonin dropped from 0.72 to 0.15 μg/ml; the urinary 5-hydroxyindole acetic acid declined from 19.8 to 7.6 mg/100 ml; and the urinary tryptamine fell from 164 to 100 mg/100 ml. The tumor itself contained 0.75 μg/gm of serotonin—more than twice the normal value. At present, the patient is completely relieved of the superior vena cava obstruction and presumably is free from recurrent carcinoid according to the biochemical tests.

DR. NAEL MARTINI (New York, NY): We have always recognized that some carcinoid tumors tend to metastasize to regional nodes and distant organs pretty much the way lung carcinomas do.

Less than 2 years ago, a review of our experience at Memorial Hospital showed that carcinoid tumors may be divided into two major groups based on their histological presentation. We call them *superficially invasive* versus *deeply invasive* types, and our colleagues at the Mayo Clinic elect to call them *atypical* versus *typical carcinoids*. A carcinoid was considered deeply invasive when it penetrated halfway through the wall of the involved organ or was larger than 2½ cm in diameter. This applied to carcinoids at any site.

When the tumors were invasive, 75% metastasized and 60% of the patients died of their disease. On the other hand, less than 1% of the superficially invasive carcinoids metastasized, and there were no deaths in this group of patients.

One important difference observed was the fact that two-thirds of the carcinoids of the lung were deeply invasive. This perhaps reflects the nature of the referrals we see at our institution.

DR. JOSEPH W. PEABODY, JR. (Washington, DC): This paper is an important contribution, especially in view of the remarkable number of cases in the Mayo Clinic series. I would just like to ask how many ossifying adenomas the authors have encountered. I am aware of at least 1 documented ossifying adenoma reported from the Mayo Clinic previously* and presumably included in the authors' series. Everyone is well aware of the paper Sir Clement Price Thomas published in 1958† citing 3 of his own cases of ossifying bronchial adenoma plus 17 additional cases from the literature. In none of these patients was the suggestion of calcium detected roentgenographically. To bring the subject of ossifying adenomas up to date, I have prepared a table of cases reported in the literature.

Ossifying Bronchial Adenomas

Author	No. of Patients
Price Thomas & Morgan	3
Their review of literature	17
Subsequent reports	17[a]
Our series	6
Total	43

[a] In 7 of these patients roentgenographic calcification within the lesion confused the problem.

The amount of bone found grossly within the specimen (and it is indeed bone formation and not mere calcification) can be striking. A remarkable amount of calcific density may pervade such specimens.

We have had 6 cases of ossifying adenoma among 60 bronchial carcinoids. Although we commonly think of calcification as being synonymous with benignity, it can be fallacious in some instances, for 1 of our 6 patients with ossifying bronchial adenoma actually had lymph node metastasis. I would like to ask Dr. Okike whether he would make some comment about the Mayo Clinic experience with this particular aspect of the problem, both from the roentgenological and the pathological standpoint.

DR. BERNATZ: We appreciate the comments of the discussants. All of us have profited from them.

We are not committed to a firm separation of carcinoids into typical and atypical types, but we do recognize the more aggressive nature of the latter group. Their identification histologically from increased mitoses, spindling of cells, necrosis, and pleomorphism may not be easy in small bronchoscopic biopsies, but our basic operative attack is the same. We are conservative with the resection of the primary tumor and vigorous in our removal of metastases. Metastasis outside the thorax is unusual, having occurred in only 4 patients and in all instances more than 5 years after the initial resection. Treatment with irradiation or chemotherapy or both has not been rewarding in the past.

Dr. Faber, there were more pneumonectomies in this series than we would have expected. Practically all were done in earlier years and were dictated by extensive suppuration secondary to main bronchial lesions.

Dr. Peabody, focal calcification with or without bone formation was noted in 30% of these tumors. A suspected ominous implication of this feature was not evident.

Whether this group of tumors is related to endocrinopathies is a challenging puzzle. In 1953 one of us described patients with multiple adenomas, including a bronchial carcinoid. Although we have emphasized the morphology and treatment of carcinoids in this report, we are confident that future efforts by our associates in the biochemical laboratories will be most helpful to our understanding of the nature and activity of bronchial carcinoids and perhaps lead to improved chemotherapeutic assistance in treatment.

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*O'Keefe ME, Good AA, McDonald JR: Calcification in solitary nodules of the lung. Am J Roentgenol Radium Ther Nucl Med 77:1023, 1957

†Price Thomas C, Morgan AD: Ossifying bronchial adenoma. Thorax 13:286, 1958

Reflux Control Following Extended Myotomy in Primary Disordered Motor Activity (Diffuse Spasm) of the Esophagus

R. D. Henderson, M.B., and F. G. Pearson, M.D.

ABSTRACT **We have previously reported the results of extended esophageal myotomy and Belsey hiatal hernia repair in 21 patients. Reflux was considered to be a late complication of this operation, and gastroplasty has subsequently been added.**

Thirty-four patients have now been surgically treated, 17 with myotomy and Belsey repair and 17 with myotomy, gastroplasty, and Belsey repair. Eight of the 17 with Belsey repair developed clinical and roentgenographic signs of reflux 6 to 27 months following operation without evidence of hernia recurrence; 5 of the 8 patients have required further operation, with the addition of gastroplasty for reflux control. Seventeen patients were treated primarily by extended myotomy, gastroplasty, and Belsey repair. None of the patients who underwent gastroplasty have reflux symptoms, and only 1 shows a trace of reflux radiologically.

Primary disordered motor activity (PDMA) of the esophagus is now acknowledged as a clearly defined disease entity in which the body of the esophagus responds to a swallowed food bolus by spastic contraction. Early recognition of this disorder is attributed to Osgood [12] in 1889, and a clearer description was given by Moersch and Camp [11] in 1934. The disorder has been better defined since the advent of manometric studies [2, 15].

Although medical management using nitrates and anticholinergics has been described [3], these methods have not been very successful. The addition of esophageal dilation has been reported to improve symptoms in some patients, but the results are variable [1, 14]. Surgical myotomy of the esophagus was described by Lortat-Jacob [9] in 1950. Since that time there have been several reported series indicating that although good results are achieved with myotomy, a significant number of patients continue to have major symptoms [4, 6].

In 1974 we reported the results of extended myotomy, 6 to 10 cm above the aortic arch and into the proximal 1 cm of stomach, together with Belsey hiatal hernia repair [8]. At that time it was recognized that delayed reflux did occur: 17 of our original 21 patients had a Belsey hernia repair, and 3 of them developed reflux. Two of the 3 patients required the addition of a gastroplasty for reflux control. Because of this problem, 4 additional patients were treated primarily by extended myotomy and gastroplasty [13]. None have developed reflux, although their follow-up is of much shorter duration.

Controversy has arisen over both the extent of recommended myotomy and the use of gastroplasty as a method of reflux control [5, 7]. It is because of this controversy that our now more extensive experience is reported, in the hope that this will allow more accurate assessment of the value of this surgical approach.

Materials and Methods

Thirty-four patients with PDMA have been treated surgically. All had an extended myotomy, from 6 to 10 cm above the aortic arch to the proximal 1 cm of stomach. In the first 17 patients a Belsey hiatal hernia repair was done for reflux control, and in the second 17 patients a gastroplasty and Belsey repair were used (Figure). All patients were studied preoperatively by history, endoscopy, radiology, and manometry, and all have been followed postoperatively.

In this group of 34 patients with PDMA, 18 were women and 16 were men with an average age of 43.4 years (range, 20 to 70 years). All patients had pain, which was described as

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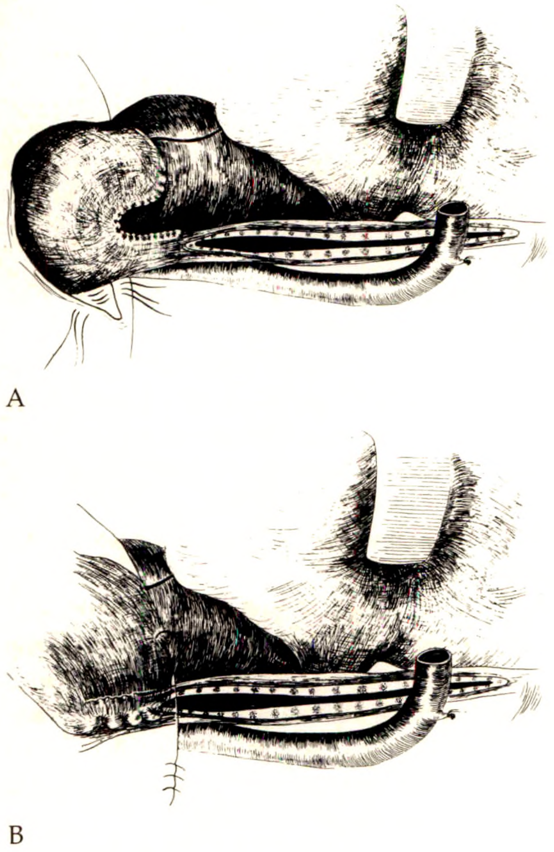

Fig 1. (A) Extended esophageal myotomy, gastroplasty, and Belsey hernia repair are performed through the left chest. The esophagus is mobilized 6 to 10 cm above the aortic arch by dividing one intercostal artery and tunneling behind the aorta. Posterior crural sutures are placed, and a gastroplasty tube is cut with a stapler, then oversewn with a continuous silk suture. The myotomy is now performed, splitting the esophageal muscle from 6 to 10 cm above the aortic arch to the proximal end of the gastroplasty tube. (B) With the myotomy completed, a Belsey hernia repair is performed that reduces the gastroplasty tube and 5 cm of distal esophagus below the diaphragm.

epigastric in 25, retrosternal in 33, and radiating to the back in 10 and to the left arm in 7. The pain was precipitated by food in 30, came on spontaneously in 13, and was related to posture in 6 and to exercise in 4. (Pain that is induced by exercise may confuse the diagnosis and raise the possibility of myocardial ischemia.) Pain relief was noted with antacids in 9 and with nitroglycerin in 3; no effective relief from medication was reported by 22 patients.

Other symptoms were reported in small numbers of patients. Eleven had reflux to the throat, with 3 of them reporting night aspirations; 10 patients burped excessively; 12 had pyrosis; 15 were nauseated; and 7 reported vomiting.

Dysphagia was the other major symptom. Thirty-one patients had food sticking at the level of the gastroesophageal junction, 6 with liquids only and 25 with both liquids and solids; 17 reported regurgitation. Food sticking at the pharyngoesophageal level occurred in 14; this happened with solids only in 4 and with liquids and solids in 10. Nine patients coughed and choked with swallowing, indicating forward spillage of the obstructed food bolus and irritation of the vocal cords.

All patients had endoscopy, but the findings were nonspecific and of no diagnostic value. Chronic epithelial changes were present, but there was no evidence of esophageal ulceration.

The radiological features of PDMA are varied and usually nonspecific. They include recognizable roentgenographic spasm in the lower two-thirds of the esophagus and evidence of thickening of the lower esophageal wall [10]. In a small number of patients, when the disease has been present for several years the proximal esophagus becomes dilated and retains food [8]. Using these criteria, a probable diagnosis of PDMA was made in 17 patients, with a thickened esophageal wall demonstrated in 8 of them. For the remaining 17 patients the radiological diagnosis was hiatal hernia in 8 and achalasia in 4; the study was considered normal in 5 patients.

Esophageal manometric studies are the most accurate diagnostic tool. The characteristic findings are a normal gastroesophageal junction with marked motor spasm in the lower two-thirds of the body of the esophagus, normal peristalsis in the upper third of the esophagus, and a normal cricopharynx and pharynx [2, 15].

All patients were studied manometrically. The tone of the gastroesophageal junction averaged 13 cm H_2O (range, 10 to 16). Relaxation was proved to be present in all but 1 patient. All patients had more than 85% of their motor waves disordered in the distal two-thirds of the esophagus, and 16 of the 34 patients studied had total disorder. The motor waves were characteristically of high amplitude and prolonged duration but did show considerable variation in amplitude. In 8 patients motor waves varied from 50 to 129 cm H_2O, in 24 the range was 15 to 49, and in 2 the motor waves averaged less than 14 cm H_2O.

Results

To describe the results of surgical treatment, it is necessary to subdivide the patients into three groups.

Group 1: 17 patients treated by extended myotomy and Belsey hernia repair

Group 2: 5 patients from Group 1 who developed severe reflux and required gastroplasty for reflux control

Group 3: 17 patients treated primarily by extended myotomy, gastroplasty, and Belsey hiatal hernia repair

Group 1

The initial approach used in surgical management was to extend the surgical myotomy 6 to 10 cm above the aortic arch and to perform a Belsey hernia repair for reflux control. Seventeen patients were treated in this manner with an average follow-up of 40 months (range, 20 to 50 months).

In these patients, 8 of the 17 (47%) developed symptomatic reflux (Table). Reflux was not recognized immediately postoperatively but developed an average of 17 months following operation (range, 6 to 27 months). In these patients reflux tended to be very severe and responded poorly to medical management. One patient with reflux moved to another province and has been lost to follow-up other than by letter. This patient continues to experience severe reflux. Two patients have been well controlled on medical management and do not require surgical treatment. Five patients remained severely symptomatic despite dietary control, bed elevation, and the use of antacids and metaclopramide. These patients were evaluated radiologically, manometrically, and endoscopically. Free radiological reflux was present in all 5, and 2 had a peptic stricture. Endoscopy confirmed the presence of reflux and again demonstrated the strictures in 2 patients. There was no radiological, manometric, or endoscopic evidence of breakdown of the Belsey repair, and a 5 cm segment of esophagus was clearly present below the diaphragm.

Not only was reflux present in 8 of the 17 patients, but the severity of the reflux was major, in 5 patients being unresponsive to standard methods of medical management. Because of this severe problem, these 5 patients were treated by gastroplasty and Belsey hernia repair. They comprise Group 2.

Group 2

At the time of operation the gastroesophageal junction was exposed and again shown to be 5 cm below the diaphragm. There was no evidence of breakdown of the original Belsey hernia repair. The addition of gastroplasty has corrected the reflux problem. These 5 patients have now been followed an average of 16 months since their second operation (range, 9 to 21 months), and none show clinical or roentgenographic evidence of reflux.

Results of the Primary Operation (34 Patients)

Group[a]	Operation	No. of Patients	No. with Reflux	Result		
				Poor	Good	Excellent
1	Myotomy & Belsey	17	8	6[b]	2	9
2	Added gastroplasty	5	0	0	1	4
3	Myotomy, Belsey, & gastroplasty	17	1	0	2	15

[a] In Group 1 reflux was the dominant problem. Group 2 represents those patients from Group 1 who required gastroplasty for reflux control. Group 3 consists of those patients who had gastroplasty and Belsey repair as their primary procedure.

[b] Five were reoperated on to add a gastroplasty; they constitute Group 2.

Group 3

Because of the experience of reflux following Belsey repair and myotomy, the operative procedure was modified to include gastroplasty and Belsey hernia repair as the method of reflux control. Seventeen patients have been treated in this manner with an average follow-up of 19 months (range, 2 to 48 months). All patients in this group have had a complete clinical and radiological follow-up. None have symptoms referable to reflux. One patient has slight radiological reflux on water-siphon study. In all patients the gastroplasty tube and the 5 cm segment of esophagus could be shown roentgenographically to be below the diaphragm.

Symptom Relief

The most important symptoms in patients with PDMA are pain, dysphagia, and reflux. The operative procedure is designed to relieve these symptoms, and its effectiveness is best judged by assessing the symptoms in long-term follow-up. As already discussed, reflux occurred in 8 of the 17 patients who had a Belsey repair and was recognized radiologically in 1 patient with a gastroplasty. Minor degrees of dysphagia are still present in 4 patients. The dysphagia is intermittent and is correctable by the passage of 60F Maloney bougie. There is no endoscopic or roentgenographic evidence of a stricture in these patients and no evidence of reflux. All 4 patients have had a gastroplasty, and in 2 this was done to correct reflux following the original Belsey repair.

The final result of treatment has been categorized as excellent in those with no residual symptoms; good in those with mild, medically controlled reflux or minor dysphagia; and poor in those with major residual symptoms. Twenty-eight patients (82%) are considered to have had an excellent outcome, 5 patients (15%) a good result, and 1 patient (3%) a poor result because of continued major reflux uncontrollable medically.

Comment

Effective control of dysphagia has been achieved by this operative approach. In previous publications the incidence of residual dysphagia has been higher [4, 6]. In our own experience, 3 patients seen in consultation and not included in this study have had major dysphagia following myotomy to the aortic arch level only. Two of them had symptomatic relief following extension of the myotomy, and 1 has required esophagectomy and colon interposition. In the 34 patients studied, residual dysphagia is present in only 4 and is mild and intermittent in each case.

Reflux has been the dominant problem. This is not entirely a new difficulty, as Ellis and coworkers [4] reported reflux in 5 of 30 patients treated by extended myotomy, 2 of whom developed a peptic stricture. Effective control of reflux in the present series has been achieved by the addition of gastroplasty. None of these patients have symptomatic reflux, while 1 of the 17 shows slight radiological reflux on water-siphon study.

The only other disease in which myotomy is commonly used for management is achalasia. In our experience the Belsey hernia repair is effective in controlling reflux in patients with achalasia [10]. There are differences between achalasia and PDMA that may account for the dissimilarity in reflux control. In achalasia the stomach has low acidity due to vagal nerve involvement, so that reflux, when it occurs, may be less noxious. With achalasia, even after myotomy there is often a residual pool of alkaline esophageal secretions and food content that will neutralize the refluxed bolus. These factors may obscure the incidence of reflux in achalasia and lessen the effects of the refluxed bolus.

There is experimental evidence [16] to support the concept that an intraabdominal esophageal segment does not prevent reflux when it is myotomized. In dog studies, when the lower esophagus and sphincter are excised and replaced by a gastric tube, the tube segment can be shown to have a tone of 15 cm H_2O. This tube segment, placed below the diaphragm, prevents reflux. When the tube is myotomized, free reflux occurs. This study, although done in dogs, indicates that a tube or segment, once myotomized and without intrinsic tone, is no longer effective in reflux control.

These theoretical considerations are of interest and help in the understanding of reflux control following myotomy. The most important consideration, however, is that among 17 patients treated by myotomy and Belsey fundoplication, reflux developed in 8 from 6 to 27 months following the operation. Control of reflux by gastroplasty has proved to be effective and is a minor addition to the operative procedure.

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Discussion

DR. F. HENRY ELLIS, JR. (Boston, MA): I have always been impressed by the superb work that has come from Toronto under the aegis of Dr. Pearson. I am afraid I will have to temper my enthusiasm momentarily in my discussion of this paper, however, for I find myself in total disagreement with almost everything Dr. Henderson has said. Two years ago, when some of this material was first presented to the Society, I had the opportunity to discuss that paper; and in reviewing my discussion of it, I find myself in the embarrassing position of having to repeat almost verbatim what I said then.

First, it seems to me that the confusion surrounding all problems concerning motility of the esophagus is such that introducing a new term to describe it only compounds the difficulties. In 1934 Moersch and Camp described the condition that they called *diffuse spasm of the esophagus.* The term is a simple one. It is an accurate one. It is widely accepted, and I hope it will continue to be.

Second, the incidence of reflux in the early group reported here, which was approximately 50%, seems excessive to me. Dr. Henderson mentions that this is a common finding in other reports in the literature and quotes one of my articles, in which he says that it occurred in 5 out of 30 patients. He refers to radiographic studies, which are notably inaccurate in documenting pathological reflux. In actual fact, symptomatic reflux occurred in only 2 of 40 patients. This may be quibbling, because 2 is 2 too many, but it does suggest that reflux may develop after a long myotomy. The reason, I think, is clear.

As Dr. Henderson points out, the lower sphincter in most of these patients not only is normal in amplitude but functions normally. Therefore, why cut it? It took me awhile to realize that the operation done for achalasia, in which the lower sphincter is at fault, should not necessarily be transferred to a condition in which the lower sphincter functions normally. One of the advantages of preoperative motility studies is to determine the function of various segments of the esophagus, and if the lower sphincter functions normally, then the incision should avoid incising it. If it is not incised, then the addition of other complicated maneuvers such as gastroplasty and the Belsey antireflux repair become unnecessary and, if used, may clearly compound and add an additional problem to an already complex situation.

In this regard, another technical point is that by using preoperative motility studies, one can identify the extent of disease, which usually involves the lower half or two-thirds of the esophagus. Rarely is it extensive enough to require an incision above the aortic arch. In those few patients in whom such an extended myotomy is necessary, it seems to me that a right-sided approach is far simpler and has the added advantage of ensuring that the lower sphincter remains intact.

Just a final word of caution about the treatment of patients with diffuse esophageal spasm: results of operation, even using the precautions I have mentioned, are not as good as those following myotomy for achalasia. The reasons for this are not entirely clear, but others who have operated on such individuals find that the success rate is more in the neighborhood of 75% than 95%. Most of the poor results when the operation is properly done are not due to reflux, but rather to the persistence or recurrence of pain. This particular problem has not yet been solved, and it needs further investigation.

DR. NICHOLAS J. DEMOS (Short Hills, NJ): I enjoyed this presentation by Drs. Henderson and Pearson very much and would like to add my comments on the part of their paper dealing with prevention of reflux.

Recurrence of reflux esophagitis is due to an intrinsic fault of many presently employed techniques. The esophagus is usually dissected out of its mediastinal bed, pulled down under tension, and held in place by sutures taken in the soft, friable, tenuous esophageal wall. If one employs the transabdominal route, the sutures that help pull down the esophagus are taken in friable esophageal wall. The same thing happens in the transthoracic Belsey repair and has been reported recently in connection with many, many recurrences—the stitches supposedly holding the esophagus under the diaphragm are inserted in friable esophageal wall.

The Collis gastroplasty was a step in the right direction for dealing with this problem. Using the lesser curvature of the stomach, the diaphragm is elongated instead of being pulled down under tension. With the Collis repair by itself, however, reflux often recurs.

Folding the stomach around the Collis gastroplasty segment provides the necessary one-way-valve mechanism as well as firm gastric tissue to anchor under the diaphragm. The sutures holding the valve area are inserted in the plicated fundic wall and the inferior surface of the diaphragm. These sutures hold well. They are not made in tenuous esophageal wall.

With the Collis-Nissen or Collis-Belsey technique, the divided fundus is resutured around the newly created esophagogastric prolongation. It occurred to us that the gastric division and resuture are superfluous. We just place a double row of staples and suture the fundus around the lower elongation of the esophagus. We have had no recurrence in the last 30 patients so treated.

DR. HENDERSON: Let me address Dr. Demos' point first. He suggests that patients who have developed reflux following myotomy are experiencing recurrence of an anatomical hiatal hernia. This is not so in our patients who have been studied. All those with reflux have been evaluated, and indeed, at the time of operation it is possible to show quite clearly that the lower 4 cm of esophagus is below the diaphragm. Thus we are not dealing with a recurrence.

Turning to Dr. Ellis' comments, I think that the name used for the disease is a matter for argument and not of great importance. Of far more significance are the issues of the techniques used and the results.

The incidence of reflux in my hands is extremely high in the absence of an anatomical recurrence. Dr. Ellis' suggestion of leaving the sphincter intact is one I have heard before. I am concerned about it because of the fact that one produces an adynamic esophagus above an intact sphincter, and I have seen this in other situations, with a myotomy above the gastroesophageal junction by itself giving rise to dysphagia. I would be most interested to see a reported series with effective follow-up using this operative approach but would be inclined to stay away from it until I have seen the results.

The incidence of dysphagia in the presently reported series is low, and I think the reason is that the myotomy was extended above the aortic arch. As I mentioned, I have seen 3 patients with a myotomy to the aortic arch level only who had residual major dysphagia and continuance of their previous pain. All 3 required further operative procedures, in 2 an extension of the myotomy while the third eventually required colon replacement of the esophagus because of intractable continuing pain.

In none of the 34 patients reported in this group has continuation of the preoperative pain been a problem. This suggests that extending the myotomy may indeed be the solution to the problem of continuance of pain that Dr. Ellis has raised.

In terms of reflux control, if one leaves the gastroesophageal junction intact, I think this by itself may well be an effective method. If one elects not to do this and to myotomize the gastroesophageal junction, certainly in my experience the incidence of reflux—8 out of 17 patients—is sufficiently high and the corrective procedure—namely, a gastroplasty—sufficiently effective that I think this is the better approach.

Dr. Ellis has suggested that his own reported series is incorrectly quoted. In his article (JAMA June 1964 [4]) he reports the results of radiological studies in 30 patients; 5 of them had demonstrable reflux, and 2 had a peptic stricture. Not all patients included in his study had radiological follow-up; however, for those studied the figures are accurate.

I very much enjoyed Dr. Ellis' comments. I think this type of discussion and argument are good for the Society.

Simplified Lateral Chest Incision for Most Thoracotomies Other Than Sternotomy

Robert Mitchell, M.D., William Angell, M.D.,
Robert Wuerflein, M.D., and Vincent Dor, M.D.

ABSTRACT **Our experience using the lateral simplified thoracotomy incision for most chest work other than operations requiring median sternotomy is reported. The incision provides adequate exposure, yet preserves major muscle masses and decreases the postoperative morbidity. Return of normal ipsilateral arm function appears to be hastened in the postoperative period. In addition, the incision is easier to open and close than the standard incision.**

Chest incisions have evolved over the past eighty years to the standard lateral thoracotomy commonly used today. In 1891 Tuffier reported resecting the apex of the right lung through the second intercostal space. G. R. Fowler in 1893 reported decortication through an elliptical vertical incision in the axillary line with the removal of 9 to 10 cm of the fifth and sixth ribs. In his paper on esophagectomy, Thorek in 1913 described approaching the esophagus through the seventh intercostal space, cutting the angles of the fourth through the seventh rib posteriorly rather than removing two ribs, which was popular in that day. In the same year Eggers reported treating empyema using a posterolateral incision similar to that utilized today. In 1924 Cutter described the median sternotomy which is popular presently for most approaches to the heart. Pneumonectomy was done in 1931 by Nissen, and large lengths of the third, fourth, and fifth ribs were removed for exposure. In this paper we describe a lateral approach that gives adequate exposure for most operations requiring entry in the pleural cavity and yet preserves much of the muscle mass in the chest.

The standard thoracotomy incision today is the posterolateral incision. Its disadvantage is that a large muscle mass must be cut, ie, the latissimus dorsi, the anterior serratus, and sometimes part of the rhomboids and the trapezius. Also, a moderate amount of time is required to open and close this extensive incision. In the immediate postoperative period, mobility of the ipsilateral arm is limited by the injured muscle mass and pain. Later in the recovery, incisional pain is more common than in most abdominal wounds. The major advantage of the posterolateral thoracotomy is the excellent exposure afforded if the intercostal space is opened in its entirety or the appropriate rib is resected from near the cartilage anteriorly to the angle of the rib posteriorly. For the past year we have used a lateral incision for most pulmonary and esophageal work and in cardiovascular operations requiring a thoracotomy incision rather than a sternotomy (Table).

Operative Technique

The skin incision extends from the nipple anteriorly to the tip of the scapula posteriorly to approach the third, fourth, or fifth intercostal space (Figure, A). The fourth intercostal space is usually used for wedge resection, lobectomy,

Operations Performed through a Limited Thoracotomy Incision

Procedure	No. of Patients
Exploratory thoracotomy	5
Transthoracic hiatus hernia repair	3
Pneumonectomy	2
Lobectomy	8
Wedge resection	12
Exploratory thoracotomy for trauma	5
Patent ductus arteriosus	20
Vascular ring	2
Coarctation of aorta	10
Mediastinal tumors	4
Recurrent pneumothorax	10

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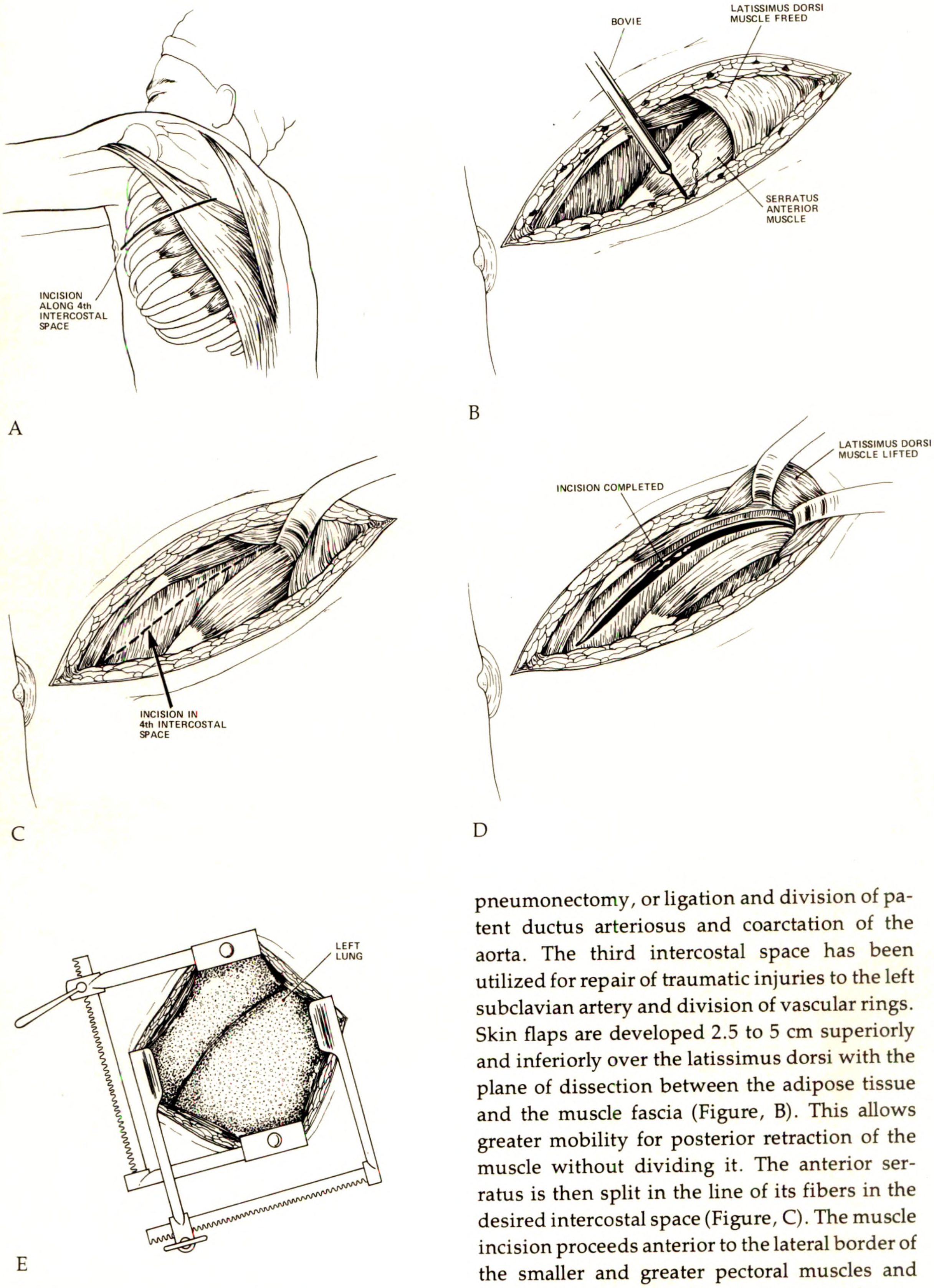
INCISION ALONG 4th INTERCOSTAL SPACE
A
BOVIE
LATISSIMUS DORSI MUSCLE FREED
SERRATUS ANTERIOR MUSCLE
B
INCISION IN 4th INTERCOSTAL SPACE
C
INCISION COMPLETED
LATISSIMUS DORSI MUSCLE LIFTED
D
LEFT LUNG
E

Technique for creating a simplified lateral chest incision. (See text for details.)

pneumonectomy, or ligation and division of patent ductus arteriosus and coarctation of the aorta. The third intercostal space has been utilized for repair of traumatic injuries to the left subclavian artery and division of vascular rings. Skin flaps are developed 2.5 to 5 cm superiorly and inferiorly over the latissimus dorsi with the plane of dissection between the adipose tissue and the muscle fascia (Figure, B). This allows greater mobility for posterior retraction of the muscle without dividing it. The anterior serratus is then split in the line of its fibers in the desired intercostal space (Figure, C). The muscle incision proceeds anterior to the lateral border of the smaller and greater pectoral muscles and posterior to the long thoracic nerve on the anterior serratus. The anterior serratus is easily lifted off the ribs posteriorly and the greater pectoral likewise anteriorly.

Usually the chest is opened through the intercostal space; however, a rib may be resected if desired. It is most important that the intercostal space be opened in its entirety, ie, from just lateral to the sternum to the rib angle posteriorly (Figure, D). This is accomplished by lifting up the muscles with a medium-sized Richardson retractor anteriorly and subsequently posteriorly and cutting the intercostal muscles with the Bovie cautery. A medium-sized rib retractor is inserted and partially opened, and the intercostal muscle division may be completed. A second rib retractor is then inserted in the opposite direction for retraction of the greater pectoral anteriorly and the latissimus dorsi in the posterior direction (Figure, E).

Comment

The advantages of the incision benefit both the patient and the surgeon. For the surgeon, less time is required to open and close the chest, as it is essentially a muscle-splitting and retracting incision rather than a muscle-dividing incision. Also, retraction of the muscle mass posteriorly draws the scapula posteriorly, keeping it from protruding into the wound. Both children and adult patients achieve earlier mobility of the arm with less pain.

The lateral incision described provides a little less exposure than the standard posterolateral thoracotomy but is quite adequate if performed with proper mobilization of the latissimus dorsi and complete exposure of the intercostal space. Certainly, the surgeon's performance of the operation should never be compromised by a limiting incision. We have extended the incision in patients with traumatic tears of the descending thoracic aorta or traumatic aneurysms of the aorta in whom dissection is required around the arch and distal aorta. This is easily accomplished by cutting the latissimus dorsi and anterior serratus muscles posteriorly, and the rhomboids and the trapezius if necessary, resulting in the standard incision.

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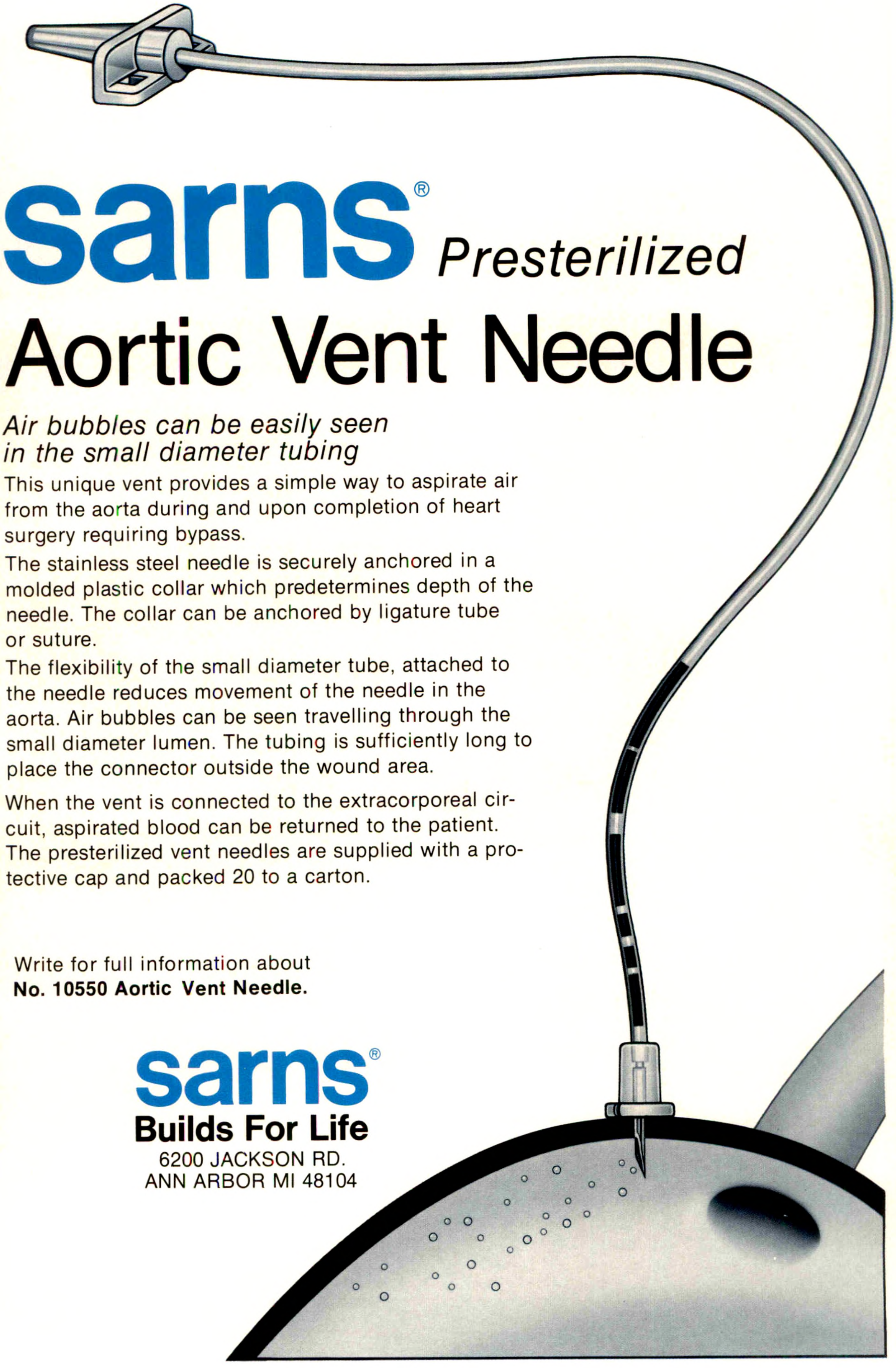

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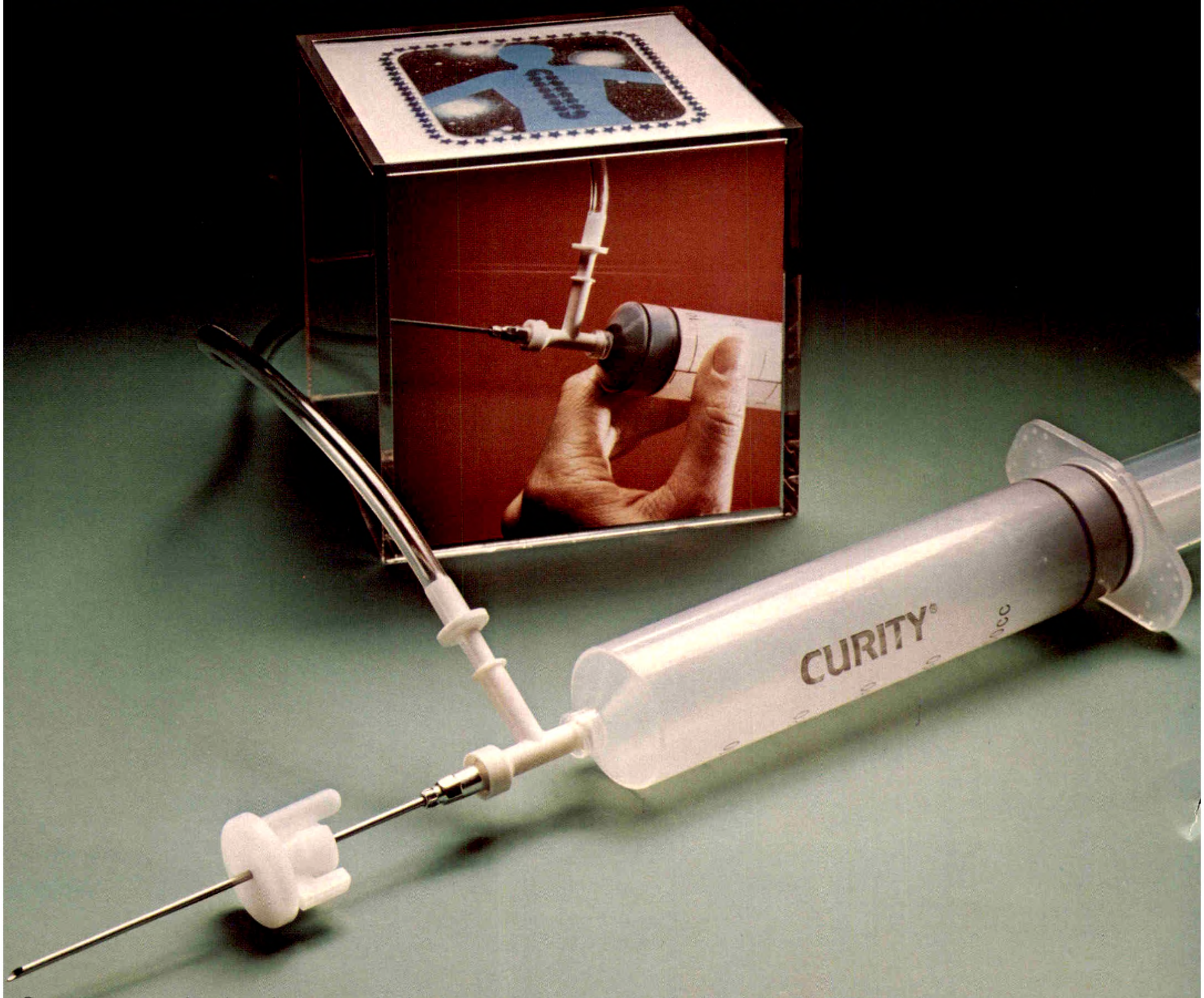

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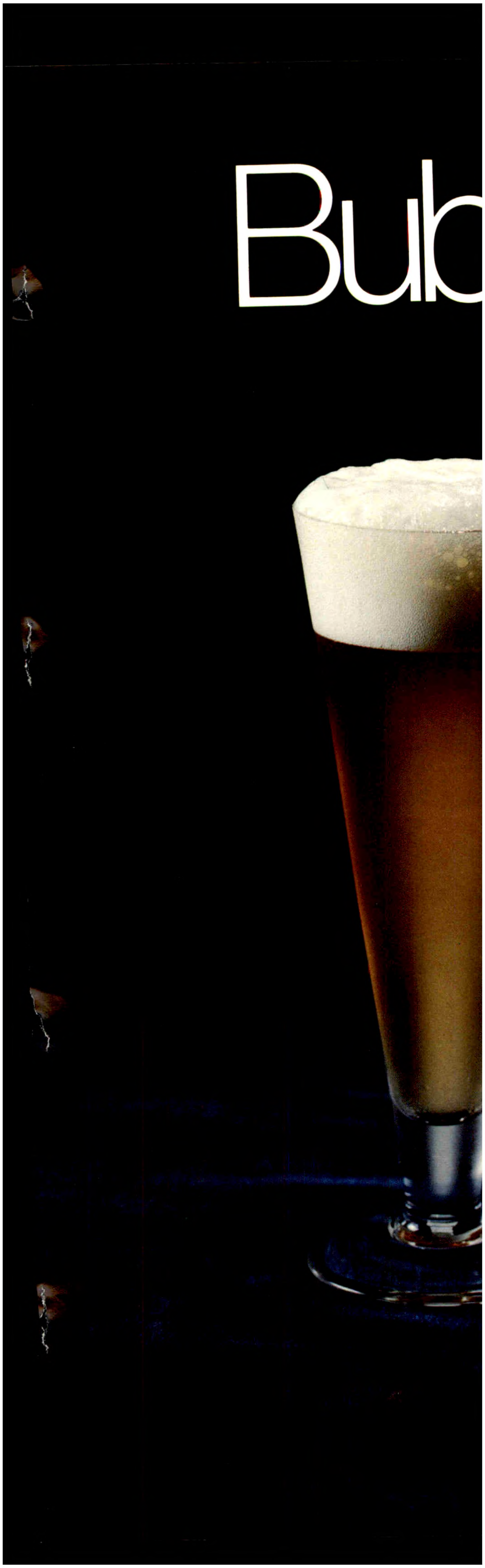
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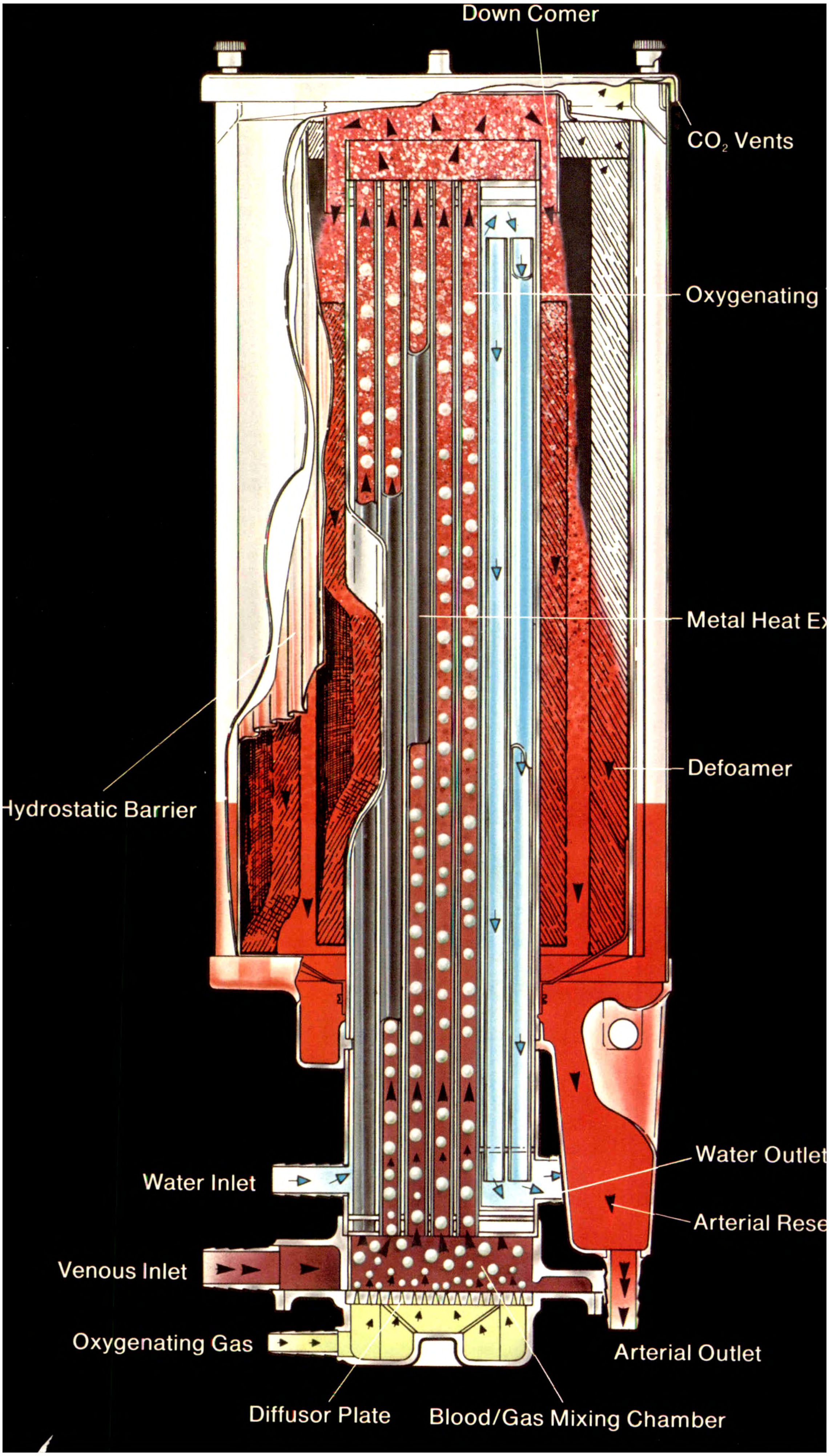
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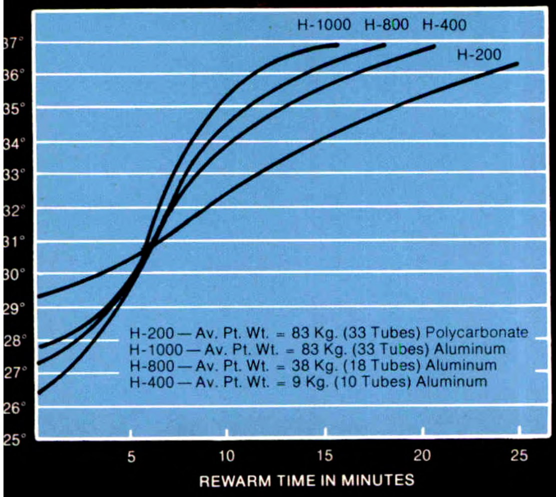

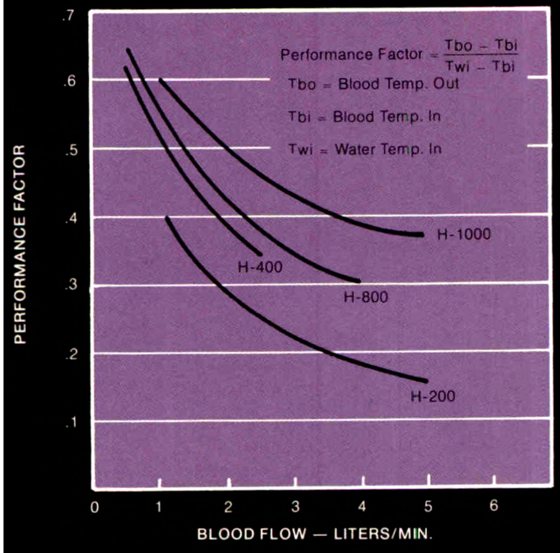

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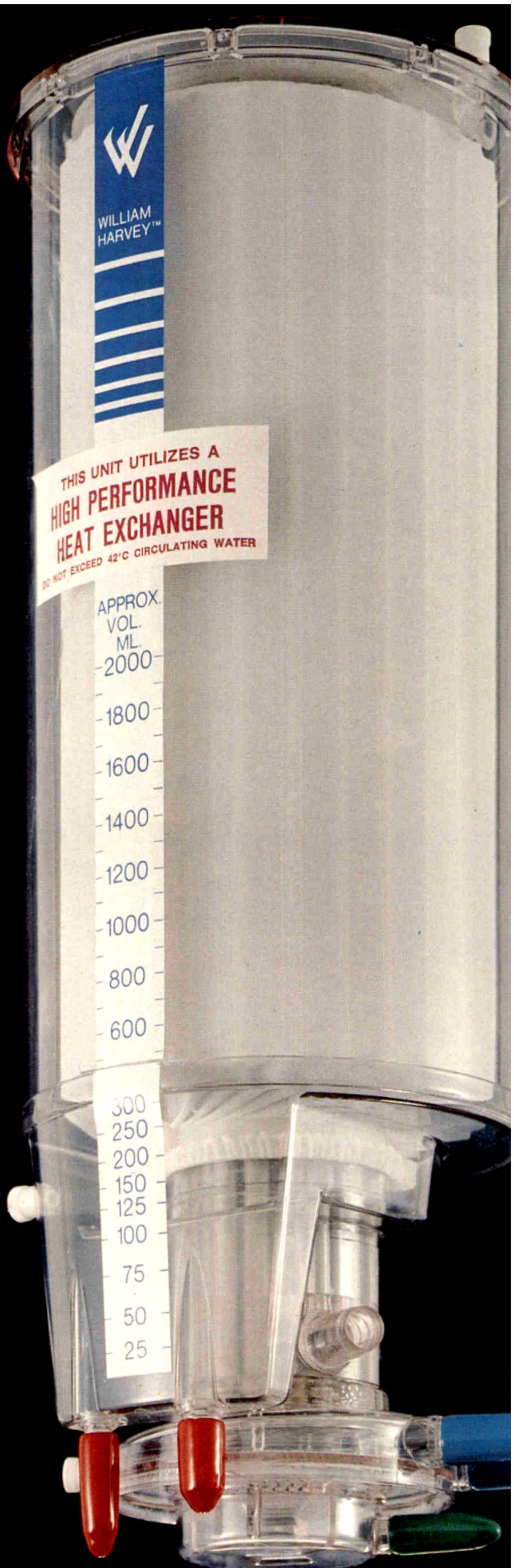

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CASE REPORTS

Vertical Axillary Thoracotomy: A Functional and Cosmetically Appealing Incision

Oscar R. Baeza, M.D., and Eric D. Foster, M.D.

ABSTRACT **Vertical axillary thoracotomy offers the specific advantages of minimum trauma and maximum preservation of chest wall function. A cosmetically acceptable scar results. The vertical axillary thoracotomy is specifically indicated in patients requiring less than the maximum intrathoracic exposure provided by the more traumatic posterolateral or anterolateral thoracotomy. The surgical technique is presented.**

Standard posterolateral and anterolateral thoracotomy incisions provide excellent exposure of the intrathoracic structures. Disproportionate chest wall injury may be inflicted by these transverse incisions in relation to the intrathoracic exposure required in certain cases, however [1]. Vertical axillary thoracotomy offers an alternative entry into the thoracic cavity that results in a minimum of trauma and thus preserves maximum chest wall function. Moreover, the vertical skin incision gives a cosmetically satisfactory result, with the scar covered by the arm.

Interest in vertical thoracotomy has been demonstrated abroad by descriptions in foreign publications of surgical technique and application [2–5, 7]. In contrast, the North American literature routinely advocates a transverse incision for axillary thoracotomy [6, 8].

Technique

The patient is placed in the lateral decubitus position with the arm abducted to 90 degrees and secured with a padded armboard (Fig 1).

The vertical incision is performed from the level of the third rib, following the midaxillary line. The subcutaneous tissue and the superficial and deep fascial layers are incised until the anterior serratus muscle is exposed. Anterior and posterior skin flaps are developed. Hemostasis is obtained with the electrocautery. The anterior serratus muscle is divided vertically, preserving the long thoracic and intercostobrachial nerves (Fig 2). The latissimus dorsi and the posterior portion of the divided anterior serratus muscle are retracted along with the scapula. The anterior portion of the anterior serratus and the greater pectoral muscle are drawn forward. The periosteum of the selected rib is then incised with the cautery and lifted off superiorly. The pleural cavity is entered through the rib bed transversely; if required, the rib may be resected. The chest wall structures are retracted to expose the intrathoracic organs.

After chest drains are placed, closure of the thoracotomy is begun by rib reapproximation. Holes are drilled in the rib below the intercostal incision, and No. 2 chromic catgut sutures are passed through the holes and around the rib above the intercostal incision, then tied. Troublesome trapping of the costoneurovascular bundle is thereby avoided. The intercostal and anterior serratus muscles are closed with continuous sutures of 0 chromic catgut. The subcutaneous tissue is approximated with a continuous suture of 3-0 plain catgut, and the skin is closed with 4-0 nylon. A pressure dressing is then applied.

Indications

Vertical axillary thoracotomy is indicated for:

1. Open lung biopsy; pleurodesis and resection of pulmonary blebs; ligation or division of a patent ductus arteriosus; pulmonary resection; and thoracic sympathectomy.
2. Patients with severe limitation of cardiopulmonary reserve.
3. Athletes requiring thoracotomy.
4. Children and women, in whom the cosmetic result is a consideration.

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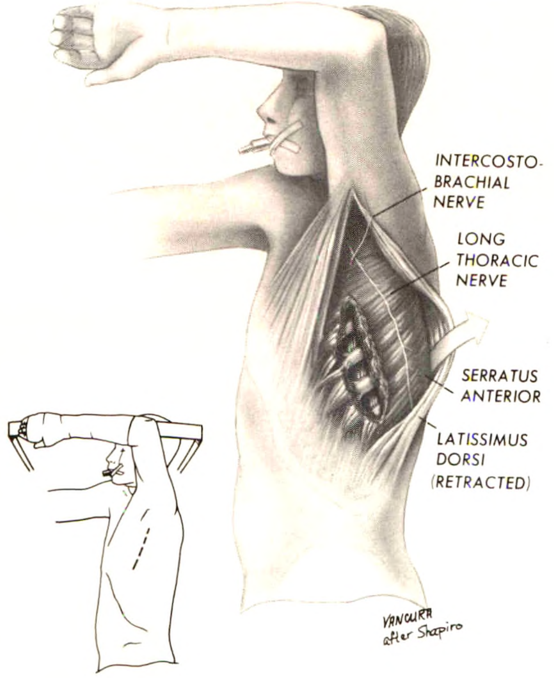

Fig 1. Patient position and surgical anatomy for vertical axillary thoracotomy.

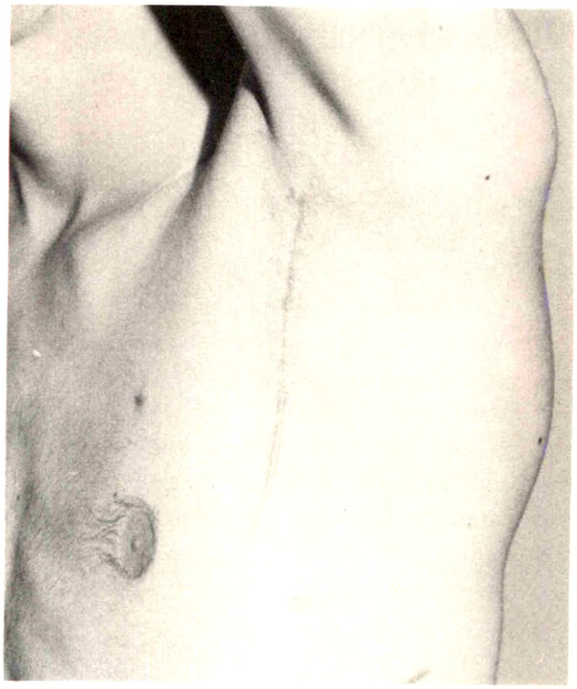

Fig 2. Postoperative result of a vertical axillary thoracotomy.

Comment

The vertical axillary thoracotomy provides adequate exposure for a wide variety of surgical procedures. Its limitation consists of restricted access to the posterior costophrenic angle. Dividing the anterior serratus vertically while preserving the nerve supply, then retracting it posteriorly with the latissimus dorsi and the scapula gives adequate access to the ribcage, thus avoiding major injury to the chest wall. The anterior aspect of the anterior serratus, which is attached to the ribcage, may be divided in the line of the fibers if an extension of the thoracotomy is needed (Fig 1). Shortened operative time, diminished blood loss, decreased postoperative pain, and rapid functional recovery are characteristic of this incision.

Our experience in children and adults has been that wound healing of a vertical axillary incision is excellent despite the fact that the incision passes perpendicular through Langer's lines (Fig 2). A vertical axillary thoracotomy as described provides adequate intrathoracic exposure for a variety of surgical procedures, with less chest wall trauma than is produced by the standard lateral thoracotomy, and results in a cosmetically satisfactory scar.

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Total Spinal Anesthesia: A Rare Complication of Intrathoracic Intercostal Nerve Block

Charles W. Otto, M.D., and Conrad L. Wall, M.D.

ABSTRACT **Total spinal anesthesia following intrathoracic intercostal nerve blocks with bupivacaine performed for postoperative pain relief during thoracotomy is described. Possible mechanisms for this complication include: (1) inadvertent placement of the needle through an intervertebral foramen, (2) puncture of a long dural cuff, and (3) intraneural injection with central spread. Recognition of this potential complication is important, and facilities for proper support must be available.**

Intraoperative intercostal nerve block for postoperative pain relief following thoracotomy has recently regained acceptance with the introduction into clinical practice of the long-acting local anesthetic bupivacaine. Although intercostal block using Efocaine* was once a popular technique, it fell into disfavor because of the high incidence of severe neurotoxic complications [4, 15]. A similar method using 1% lidocaine in 10% Dextraven (10% dextran and 5% glucose in water) with 1:250,000 epinephrine was described in the early 1960s [12, 13] but did not gain widespread popularity.

Recently, total spinal anesthesia following intraoperative intercostal block was reported [2]. The purposes of this communication are to describe another occurrence of this event and to review the possible mechanisms involved.

A 51-year-old woman, ASA Class II, weighing 92 kg, had had internal and external irradiation followed by an abdominal hysterectomy and bilateral salpingo-oophorectomy for endometrial carcinoma. A chest roentgenogram revealed a mass in the right cardiophrenic angle, and a right lateral thoracotomy was scheduled. Preoperative medication consisted of morphine sulfate, 4 mg, pentobarbital, 150 mg, and atropine sulfate, 0.4 mg, given intramuscularly one and one-half hours before induction of anesthesia.

Anesthesia was induced intravenously with sodium thiopental (500 mg in divided doses), halothane, and oxygen. Intubation with a left-sided Robertshaw double-lumen tube was facilitated by succinylcholine, 120 mg intravenously, after 4 ml of 4% lidocaine had been administered by laryngotracheal spray. Maintenance anesthesia consisted of 0.5% halothane with 50% nitrous oxide and oxygen. Muscle relaxation was produced by intravenous administration of pancuronium bromide (4 mg total), monitored by peripheral nerve stimulation. The anesthesia was uncomplicated throughout the first two and one-half hours. Blood pressure and pulse ranged from 86 to 90/60 torr and 70 to 90 beats per minute, respectively. Ventilation was controlled throughout.

Following removal of a benign pericardial cyst and before the chest was closed, approximately 8 ml of 0.5% bupivacaine was injected into each of the intercostal nerve bundles of the sixth, seventh, and eighth ribs. A 22-gauge needle was inserted approximately 4 cm lateral to the transverse process and advanced parallel to the intercostal nerve bundle for about 1 cm; the injection was done during withdrawal. No change in vital signs was noted during this time.

Following closure of the thoracic cavity and establishment of chest tube suction, neostigmine, 2.5 mg, and atropine, 1.0 mg, were given intravenously to reverse the neuromuscular blockade. Fifteen minutes later the patient was still apneic and unable to sustain a response to tetanic stimulation. Neostigmine and atropine were repeated in the same dosage, and 15 min-

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*A solution of 1% procaine, 0.25% procaine hydrochloride, and 5% butyl-p-aminobenzoate in 2% polyethylene glycol 300 and 78% propylene glycol.

utes later there was sustained response to tetanic stimulation but apnea persisted. The pupils were fixed and dilated.

All anesthetic agents were discontinued. The remainder of chest closure was quickly concluded. As the patient was returned to the supine position, the pulse dropped to 55 beats per minute and blood pressure was undetectable. Intravenous administration of ephedrine, 25 mg, and atropine, 0.4 mg, resulted in a blood pressure of 120/70 torr and pulse of 90 per minute with no further cardiovascular instability. Neurological examination at this time revealed complete flaccidity of all muscle groups, absent deep tendon reflexes, and complete lack of response to nociceptive stimuli. Funduscopic examination was normal. The Robertshaw tube was replaced with a single-lumen, soft-cuffed endotracheal tube under direct vision without patient response. The patient was then transferred to the postanesthetic recovery room and mechanically ventilated.

Approximately 20 minutes following her arrival in the recovery room (100 minutes after the intercostal blocks), spontaneous movements of the patient's head and neck were noted, and within the next 10 minutes she was able to follow simple commands with eye movements, head nodding, and a weak hand grip. A distinct sensory level at T2 could be demonstrated by pinprick at this time. One hour later the pupils had returned to normal size, and there were weak movements of all extremities. Spontaneous respiration had returned but was shallow, and assisted ventilation was continued. After another hour, upper extremity motor power was good but the lower extremities were still weak, and a T10 sensory level was demonstrated. Spontaneous ventilation was judged adequate, and she was administered humidified oxygen through the endotracheal tube. Two and three-quarter hours after the first return of movement (265 minutes after the blocks), there was a sensory deficit in the distribution of the nerve blocks only, and motor power was fully recovered. She was extubated and transferred to the surgical intensive care unit. The remainder of her hospital course was uncomplicated, and she was discharged on the seventh postoperative day. During the postoperative visit no residual central nervous system effects were found, and she had only a very vague memory of events in the recovery room.

Comment

Although the onset of spinal anesthesia was not heralded by a change in blood pressure or pulse in this case, the cardiovascular instability seen with position change, failure to regain consciousness, areflexia, fixed and dilated pupils, persistent apnea, clear-cut sensory level on regaining consciousness, and rapid, complete recovery are all consistent with the conclusion that total spinal anesthesia resulted from the intercostal nerve blocks performed under direct vision. In addition, the total duration of block (265 minutes) is similar to that found when bupivacaine is used for spinal anesthesia [5], and the time to recovery of consciousness, motor function, and sensation is similar to that seen when inadvertent total spinal anesthesia occurs during attempted epidural block with bupivacaine [9]. Peridural and total spinal anesthesia has been reported as a complication of nearly every type of paravertebral somatic or sympathetic nerve block [1, 8, 11, 14, 16, 17, 20, 21]. The possibility of total spinal anesthesia during epidural and caudal anesthesia [9, 10, 16, 17, 19] is well known. However, only 1 case of total spinal anesthesia resulting from intercostal nerve block under direct vision has been reported [2].

Subarachnoid deposition of bupivacaine under these circumstances could occur from inadvertently placing the needle through an intervertebral foramen or from puncturing a long dural cuff. However, direct subarachnoid injection is not necessary. It has been demonstrated that peripheral intraneural injections of radioactive substances [3], radiopaque contrast agents [7], finely ground carbon [7], and methylene blue in Efocaine [18] or lidocaine [19] can result in these markers being found in the spinal cord and subarachnoid space. Central spread occurs along connective tissue spaces formed by the dense perineurium surrounding individual nerve fasciculi as far proximal as the dural penetration of the nerve. At the dural penetration the perineurium becomes continuous with the dura mater, and the nerve roots continue into the spinal cord with only a thin layer of pia mater surrounding them. Injected materials reach the subarachnoid space by two routes. Commonly, the force of injection causes the fragile pia mater to rupture, causing sudden widespread subarachnoid dissemination [16, 19]. In some cases the injected material may pass along the nerve roots beneath the pia to spread up and down the spinal cord. When this occurs using methylene blue as the marker, light staining of the spinal fluid is seen in 10 to 15 minutes and heavy staining only after 35 to 40 minutes [15]. If the local anesthetic in solution follows the same path (central spread with diffusion through the pia), this might explain those cases of slow or late onset of total spinal anesthesia following peripheral nerve block.

Intraneural injection with central spread is not easily accomplished even with direct visualization of the nerve. When the needle point is placed at or near the center of a nerve fasciculus, injection may be as easy as an intravenous injection, and central spread occurs readily [7]. However, with the needle in any other position there is considerable resistance to injection, and injected substances collect beneath the epineurium without central spread [3]. This difficulty may explain why total spinal anesthesia is such a rare complication of peripheral nerve block and why it may be seen more frequently when the nerve block is performed under direct vision.

Other factors that may influence the induction of total spinal anesthesia under these circumstances include the patient's position, the specific gravity of the injected solution, and the volume and speed of injection. Commercial bupivacaine has a specific gravity of approximately 1.006 at 37°C [10], making it isobaric to spinal fluid in most individuals. Therefore, spread of the solution will be little affected by patient position. In experimental conditions, volumes as small as 0.5 ml may reach the cerebrospinal fluid if the needle is properly positioned [3]. Should the solution reach the subarachnoid space, the larger the volume injected, the more profound will be the ensuing block. A rapid injection is more likely to lead to increased spread of the anesthetic agent either within or outside the subarachnoid space.

Conclusion

Although intraoperative intercostal block is a valuable technique for relieving postoperative pain, the potential for producing the rare complication of spinal block must be recognized, and facilities for proper support need to be available. Total spinal anesthesia causes loss of consciousness, complete motor paralysis, and loss of vasomotor control. None of these need be catastrophic. Indeed, total spinal anesthesia has been utilized as a planned anesthetic technique with favorable results [6]. In the context of intraoperative blocks, the patient is already unconscious and frequently paralyzed, so that respiration is being controlled. Since cardiovascular function is being monitored closely, a drop in blood pressure or pulse should be detected quickly and can be readily corrected by the administration of intravenous fluids and vasopressors if necessary.

A few simple precautions may help to minimize the possibility of this complication. Injection should be made as far lateral to the spine as possible. Aspiration should precede injection. The volume injected should be the minimum needed to accomplish the block. The injection should be made slowly. If total spinal anesthesia occurs in spite of these precautions, pharmacological support of the cardiovascular system as needed and mechanical support of respiration until the patient recovers from the block are essential.

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Editor's Note

The possibility of this complication was one of the first things I learned when I entered the field of thoracic surgery in 1947, but it deserves reemphasis.

Massive Pulmonary Embolism Permitting Paradoxical Systemic Arterial Embolism: Successful Surgical Management

Richard C. Shaw, M.D., Philip A. Ludbrook, M.D.,
Alan N. Weiss, M.D., and Clarence S. Weldon, M.D.

ABSTRACT **The case of a young woman, receiving oral contraceptives, who developed massive pulmonary embolism producing circulatory collapse and paradoxical arterial embolism through a patent foramen ovale is documented. Limb viability was threatened. Emergency management included removal of arterial and pulmonary emboli, surgical closure of the patent foramen ovale, inferior caval partitioning, ovarian vein ligation, and short-term anticoagulation. Recovery was rapid and complete.**

Paradoxical thromboembolism refers to a situation in which a thrombus generated in the venous system is transported to the arterial system by way of large venoarterial communications. For many years it has been recognized as a complication of congenital heart disease in which there is right-to-left shunting. It has been acknowledged also as a complication of arteriovenous malformations. More recently a syndrome has been identified in patients with persistent patency of the foramen ovale who suffer pulmonary thromboembolism [4]. In these patients, pulmonary arterial blockade produces acute elevation of right ventricular and right atrial filling pressures while reducing filling pressure in the left atrium. A reversal of the normal interatrial gradient favors right-to-left intracardiac shunting and permits embolization to the systemic arteries. It is speculated that the production of acute right atrial hypertension following massive pulmonary embolism might even result in enlargement of a small existing patent foramen ovale or permit reopening of a previously closed fossa ovalis.

This syndrome has seldom been recognized during life even though pulmonary embolism is commonplace, and considering the incidence of patency of the foramen ovale, the population at risk for paradoxical embolism is large. Recently we have successfully managed a patient with this syndrome. The woman presented in extremis and was managed by an extensive surgical procedure including: removal of emboli through the left brachial, right femoral, and left femoral arteries; surgical closure of a large patent foramen ovale; removal of emboli from both the right and left pulmonary arteries; plication of the inferior vena cava; and ligation of the ovarian veins.

A 25-year-old woman was transferred to Barnes Hospital in January, 1975, because of an abnormal aortogram. She had been in good health until the previous month, when she suffered the sudden onset of shortness of breath, wheezing, and pleuritic type chest pain. She was initially treated elsewhere with bronchodilators, but the shortness of breath became progressively worse. In early January she noted numbness of her lower extremities and was hospitalized. She received no specific therapy and was discharged ten days later. Three days following hospital discharge she experienced lower abdominal tenderness followed by left chest pain and was readmitted to the hospital. She had been receiving oral contraceptives for several years, was mildly obese, and had a sedentary job as a telephone switchboard operator.

At that time examination had revealed tachycardia, tachypnea, and a low-grade fever. Mild peripheral cyanosis in the extremities was noted, and there were no palpable pulses in the left arm. The chest roentgenogram and the electrocardiogram were interpreted as normal. The next day she complained of pain in both legs,

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which were noted to be cyanotic and pulseless. An aortogram was performed that demonstrated embolic occlusion of the origin of the left subclavian artery of the infrarenal abdominal aorta. She was transferred to the Barnes Hospital.

Emergency embolectomies under local anesthesia were performed through the left brachial, left femoral, and right femoral arteries. An enormous number of old and recent blood clots were removed from all three locations. Intravenous heparin therapy was instituted following the embolectomies. Over the next several hours pulses in the extremities, which had been restored at the time of embolectomy, remained palpable, but the patient's condition grew worse, with increasing dyspnea, generalized cyanosis, tachycardia, and hypotension. She was then noted to have an abnormally loud second heart sound at the base of the heart, and a diagnosis of pulmonary arterial hypertension was made. It was suspected that the patient had had pulmonary emboli that had produced paradoxical embolism.

An emergency cardiac catheterization was performed. Arterial Po_2 was 43 mm Hg, a saturation of only 78%. Cardiac output was markedly reduced, with an arteriovenous oxygen difference of 7.2 vol per 100 ml. Pulmonary vascular resistance was calculated at 800 units, and pulmonary artery and right ventricular pressures were 70 mm Hg. The mean right atrial pressure was 5 mm Hg, and pressure in the left atrium, which was entered by way of the patent foramen ovale, was 1 mm Hg. There was a significant stepdown in oxygen saturation from the pulmonary veins (86%) to the left atrium (75%). An injection of contrast material into the right side of the heart revealed multiple large pulmonary emboli, streaming of contrast material from the right atrium to the left atrium across a persistent foramen ovale, and a normal internal appearance of the left atrium and left ventricle with nothing to suggest a source of emboli in the left side of the heart.

The patient remained markedly hypotensive and was taken immediately to the operating room, where, through a median sternotomy, her pale, acutely failing, massively dilated heart was exposed. Cardiopulmonary bypass was instituted. The 2 cm patent foramen ovale was closed with interrupted sutures through a right atriotomy. Following closure of the foramen ovale a pulmonary arteriotomy was made, and a large amount of old and fresh emboli was evacuated from both pulmonary arteries. Additional emboli were removed by squeezing both lungs and forcing clots from the smaller pulmonary arteries back into the main pulmonary arteries. When normal circulation was restored, the central cardiac pressures and saturation of blood obtained from a peripheral artery were normal. An abdominal midline incision was made, a clip was placed on the inferior vena cava, and both ovarian veins were exposed and ligated. The ovarian veins appeared normal.

Her postoperative course was unremarkable. She was maintained on heparin therapy for a two-week period and then discharged from the hospital. The patient has remained asymptomatic during the seventeen months following her operation.

Comment

Paradoxical embolism has been regarded as a medical oddity, and the diagnosis ordinarily has been made at postmortem examination. In 1971, Meister and colleagues [4] documented 5 patients in whom such a diagnosis was made during life and pointed out that among 128 previously reported patients, only 12 had had the diagnosis made antemortem. Diagnostic criteria have been established by Gazzaniga and Dalen [2] and by Gleysteen and Silver [3]. These include three features: demonstration of a venous source for the emboli, whether by clinical manifestations of thrombophlebitis or presumptive evidence provided by the occurrence of pulmonary embolism; a connection between the peripheral venous and peripheral systemic arterial circulations providing a potential right-to-left shunt, which in the case of intracardiac shunts requires a reversal of the normal pressure relationships; and finally, the occurrence of proved systemic embolization without a source of emboli in the pulmonary veins, the left atrium, or the left ventricle. These authors pointed out that the key to making the diagnosis is entertaining it as a diagnostic possibility.

The review by Edwards and co-workers [1] of 82 cases of peripheral arterial embolism demonstrated that the source of the emboli was the left side of the heart in 94% of the cases. Considering this study, Meister's group observed that in the absence of mitral stenosis, atrial fibrillation, or myocardial infarction, the probability that the emboli originate in the left side of the heart is small, and paradoxical embolism from the venous circulation should be suspected. Scammon [6] and Thompson [7] and their associates studied the incidence of patency of the foramen ovale in the general adult population and concluded that the foramen is at least probe patent in 25 to 35% of the adult population. The majority of reported cases of paradoxical embolism have occurred by way of a patent foramen ovale. Padula and Camishion [5] emphasized the requirement for abnormal pressure elevation in the right side of the heart in the pathophysiology of paradoxical embolism, and they noted that although approximately 80% of paradoxical embolization is associated with previous pulmonary emboli, elevation of right-sided heart pressures also occurs in chronic obstructive lung disease and a variety of pulmonary infections. It is possible, moreover, that sudden elevation of right atrial pressure may produce acute enlargement of a small, persistently patent foramen ovale or even open a previously closed fossa ovalis. Thus, the population at risk for paradoxical embolism is a combination of those susceptible to pulmonary embolism and those with persistent patency of the foramen ovale as well as other forms of intracardiac or venoarterial communications. The population at risk is almost certainly relatively large and the occurrence of the syndrome more common than the earlier literature had suggested.

It is not possible to establish uniform guidelines for managing patients with pulmonary embolism that might permit paradoxical embolism. It is probably true that management should be variable and related to symptomatology. Anticoagulation with intravenously administered heparin should be employed unless specifically contraindicated. Arterial embolectomy should be done whenever the viability of function of the affected part is threatened. The indications for pulmonary arterial embolectomy remain shock and circulatory collapse. The value of caval ligation and partitioning in the control of continued embolization is not precisely established. Surgical closure of a persistent foramen ovale should be considered whenever reversal of the normal pressure gradient between the right atrium and left atrium persists. Such a reversed gradient, of course, will continue only in the presence of severe blockade of the pulmonary circulation. If the cause of the blockade is pulmonary emboli, these can be removed at the time of surgical closure of the foramen ovale.

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Pulmonary Embolism and Intracardiac Shunt: A Unique Indication for Operation

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ABSTRACT **Pulmonary embolism with right-to-left intracardiac shunt presents a special problem for the clinician. A review of the literature and 4 personal cases, all diagnosed antemortem, are presented. On the basis of this information certain conclusions are drawn, and we suggest the problem to be a unique indication for the consideration of surgical intervention.**

Considerable disorder and controversy remain in surgical thinking concerning the indications for operative treatment of pulmonary embolism. The extremes range from prevalent use of inferior vena caval interruption to essentially no surgical intervention whatsoever. The usual criterion for performing pulmonary embolectomy utilizing cardiopulmonary bypass has been nonresponsive hypotension. Vena caval interruption is suggested when anticoagulation is contraindicated, if embolization occurs during adequate anticoagulation therapy, when the emboli are septic, and following pulmonary embolectomy. Recent work on the hemodynamic effects of pulmonary embolism has been presented by McIntyre and Sasahara [29], who have stressed again the importance of prior cardiopulmonary disease and emphasized the work of Haggart and Walker [18] and of Dalen and associates [4] regarding right ventricular failure. Moreover, they have provided the clinician with a framework for an orderly approach to specific surgical indications.

We propose to make a contribution by reporting our experience with pulmonary embolism and right-to-left intracardiac shunt and to echo Meister and co-workers [32] and Meade [31] that this combination with paradoxical embolism is much more prevalent than would be judged from the relative paucity of articles in the literature. We suggest that the demonstration of an intracardiac shunt with pulmonary embolism may be an additional indication for surgical treatment.

Paradoxical Arterial Embolism

Paradoxical embolus, an arterial embolus that originates in the venous system, has been well documented in both old and recent literature. Johnson [26] referred to the earliest reports of Cohnheim (1877) in the German literature and Zahn (1881 and 1885) in the Swiss when tabulating 40 cases and adding 3 of his own. In more recent literature Gazzaniga and Dalen [15], Gleysteen and Silver [16], and Meister and colleagues [32] have reviewed the subject. Meister's group tabulated 128 cases, 12 having been diagnosed during life, and added 4 additional patients to this group (2 with congenital heart disease and 3 with patent foramen ovale; 1 of the original 12 patients was theirs). Following vena caval interruption, 2 of their patients did well and 2 died of cerebral infarction. The fifth patient, who had an atrial septal defect, had no definite systemic emboli and did well with heparin therapy alone.

Acute pulmonary hypertension secondary to massive pulmonary embolism is usually present as a precursor to paradoxical embolism. The likelihood of the embolus traversing the shunt to a lower-pressure circuit has been pointed out by many authors. These patients actually are in triple jeopardy from: (1) further pulmonary embolism; (2) impaction of the foramen ovale by emboli, thereby increasing the acute right heart strain already present; and (3) systemic arterial embolism. If pressure in the right atrium exceeds that in the left atrium, the hemodynamics favor passage through the shunt. Even if the embolus is quite small relative to those already in the lung, it can cause devastating damage in the cerebral circulation. There have been several reports of chronic disease characterized by recurrent pulmonary embolism and cerebral symptoms [16, 20, 22].

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Daly [5] studied venoarterial shunting in obstructive pulmonary disease. He found shunting through a patent foramen ovale in 4 of 15 patients with chronic bronchitis when contrast medium was injected into the inferior vena cava. Thompson and Evans [46] reported a clinical paradoxical embolus in a patient with chronic pulmonary disease secondary to tuberculosis.

Lauten and associates [27] suggested that pulmonary hypertension is not necessary because of a changing relationship of atrial pressure during the normal cardiac cycle. Clinical support for this impression has been provided by Thompson and Evans [46], who reported a case of pulmonary infarction without acute cor pulmonale but with sudden hemiplegia and aphasia some hours later, and by Porter [38], who reported a 26-year-old man with phlebitis and acute hemiparesis but without pulmonary embolism clinically. Jacobi and co-workers [25] noted postmortem findings in a 47-year-old woman with an anterior descending coronary artery embolus, a patent foramen ovale, and femoral vein thrombosis but without pulmonary embolism. Anderson [1] reported a 42-year-old woman in whom a hysterectomy was followed by acute hemiplegia and iliac artery embolism; she also had a patent foramen ovale without pulmonary embolism. The absence of a valvelike piece of tissue over the foramen would make this a more likely occurrence.

The intracardiac shunt is commonly a patent foramen ovale but may be an atrial or ventricular septal defect [35], patent ductus arteriosus [13, 21], or pulmonary arteriovenous malformation [23, 42]. Thompson and Evans [46] reviewed 1,100 consecutive postmortem examinations and found a patent foramen ovale in 35%. If infants less than 6 months of age are excluded, the findings were 23% with probe patency and 3% with pencil-patent foramina. The authors cited confirmatory studies by Bizot and Fawcett, whose patients were all above 10 years of age; the foramen was patent in 30 and 31%, respectively. Although the site of arterial embolism is unpredictable, a common denominator in all reports of paradoxical embolism is the high incidence of cerebral embolus, particularly to the middle cerebral artery. In a correlative observation, the same authors reviewed 13,234 consecutive postmortem examinations and found 49 instances of cerebral embolism [46]. Two of these, or 4%, were paradoxical in origin. These authors cite Wittig as having found renal artery involvement in 44.5% of patients with proved paradoxical emboli, more than one-third of them bilateral. Edwards and co-workers [11], in reviewing 82 cases of peripheral arterial embolism, reported 1 case of paradoxical embolism and pointed out the pathological peculiarities, namely, a "circular pattern of peripheral white and central red thrombus, indicative of venous origin."

The site of origin of the embolus is usually thrombus in the distal venous circulation but may be distal tumor [46] or a right atrial myxoma [17, 19]. There has been a case of foreign body (intravenous catheter) paradoxical embolus [34]. Air [9, 12, 33] and fat [28] may also pass through an intracardiac shunt into the arterial system. Associated cerebral abscess in congenital heart disease has been ascribed to this cause.

Paradoxical embolism has been reported in the neonate [21] as well as all other age groups. It is particularly common in obstetrical patients [1, 6, 7, 12, 16, 37, 40, 46, 49].

Death caused by myocardial infarction secondary to paradoxical embolus to a coronary artery has been reported numerous times [20, 25, 39, 45, 48].

Embolic Occlusion of the Shunt

Embolic occlusion of an intracardiac shunt has also been well documented. In 1859 Wallman [47] reported observing a thrombus in a foramen ovale. Elliott and Beamish [12] cited the reports of Zahn (1881) and Hansen (1888) and tabulated 48 cases in the literature, 29 of them after 1926. Of these, 13 or 14 had peripheral emboli in addition (8 were to the brain). These authors pointed out the significance of the patent foramen ovale in prolonging survival time in massive occlusion of the pulmonary arterial tree by allowing decompression of the right side of the heart. They postulated that acute impaction of another embolus might produce acute irreversible right heart strain. They also suggested that an electrocardiogram *not* showing right heart strain with massive pulmonary embolism was diagnostic of an intracardiac shunt. This was subsequently refuted by Soloff and Zatuchni [43] and others and is contradicted by our Patients 1 and 4. Corrin [2] presented 2 cases of embolic occlusion of a patent foramen ovale with multiple pulmonary emboli. Somerville and associates [44] reported a 65-year-old patient who suffered embolic impaction of both an atrial septal defect and a patent foramen ovale postoperatively following systemic embolism to a brachial artery. Davies, Muller, and Cooper [6] presented 2 additional cases: a 45-year-old woman following cesarean section and a 73-year-old man with a history of massive pulmonary embolism three months before admission who had a systemic embolus to the right leg. Both patients died with impacted thrombus in a patent foramen ovale.

Case Reports

Patient 1

In 1967 a 39-year-old man with obvious superficial thrombophlebitis following local trauma arrived in the emergency room with dyspnea and pleuritic pain. A diagnosis of pulmonary embolism was made, and right heart catheterization and pulmonary angiography were carried out.

The roentgenograms demonstrated approximately 60% obstruction of the pulmonary artery. The aorta opacified simultaneously with the pulmonary artery following injection of contrast material into the right atrium. Mean pulmonary artery pressure was 35 mm Hg. The arterial Po_2 was 47 mm Hg with the patient breathing room air. He was treated with intravenous heparin and recovered. Sixteen days after the initial study the pulmonary artery pressure had fallen to 17 mm Hg, and the arterial tree was essentially normal. He remains well nine years later.

This case represents double serendipity: accidental discovery of the shunt and possibly accidental recovery without more serious consequences. Our treatment would be different at this time.

Patient 2

In 1969 the 74-year-old father of Patient 1 had an aortic dissection confirmed by angiography. He was treated with antihypertensive medications and did well until the seventh hospital day, when suddenly he became hypotensive. It was suspected that the dissection had extended or actually ruptured. A venous angiogram, however, showed massive pulmonary embolism with approximately 60% obstruction of the pulmonary vascular tree and simultaneous pulmonary artery and aortic filling (Fig 1). The pulmonary artery pressure was 30 mm Hg. He was treated with immediate vena caval plication but died in the early postoperative period. Postmortem examination confirmed the presence of the aortic dissection, pulmonary embolism, and patent foramen ovale.

The choice of vena caval interruption in a patient with right ventricular failure was a bad one and undoubtedly contributed to his death by suddenly lowering the venous return.

Patient 3

Four days following vagotomy and gastroenterostomy for an obstructing duodenal ulcer, a 43-year-old man had a sudden syncopal episode with cardiac arrest. Successful resuscitation was carried out, but the patient remained semicomatose. Right heart catheterization and angiography (Fig 2) demonstrated greater than 50% pulmonary artery obstruction and simultaneous pulmonary artery and aortic filling. The pulmonary artery mean pressure was 36 to 52 mm Hg. The right atrial mean pressure was 10 to 20 mm Hg and right ventricular end-diastolic pressure was 22 mm Hg. The Po_2 was 41 mm Hg with the patient breathing 50% oxygen. The systemic blood pressure was maintained at 100 mm Hg with a slow metaraminol drip, and heparin was given intravenously. His cerebral status did not improve, and he died the following day. No postmortem examination was obtained.

Patient 4

A 60-year-old woman with a three-week history of superficial phlebitis was seen in the emergency room with acute left-sided hemiparesis. A diagnosis of pulmonary embolism with paradoxical cerebral embolus was made, and pulmonary angiography was carried out that revealed a large main pulmonary artery embolus and simultaneous pulmonary artery and aortic

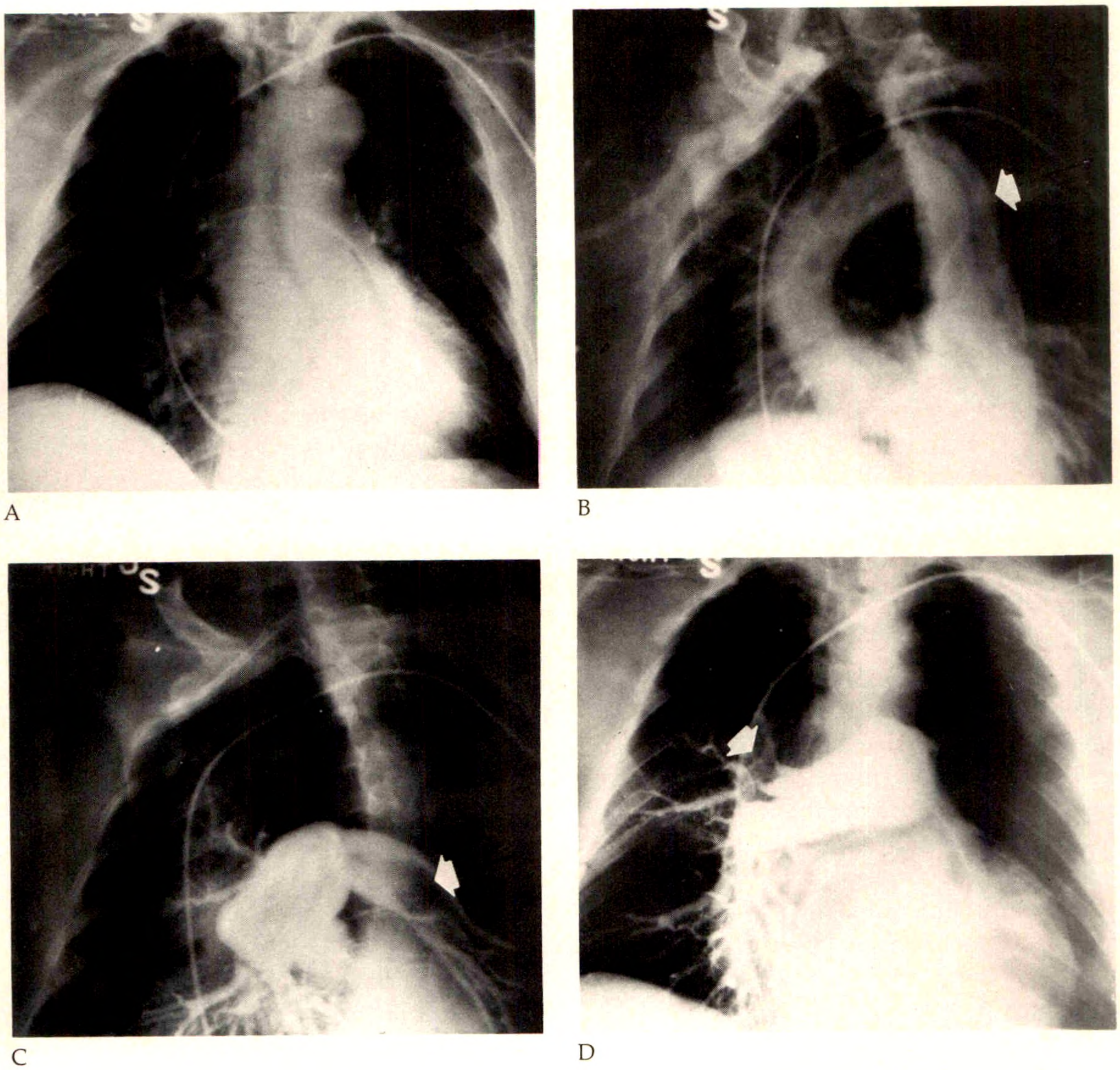


Fig 1. (Patient 2.) Seven days following this man's admission for aortic dissection, venous angiography demonstrates (top) *double aortic lumen and* (bottom) *massive pulmonary embolism.*

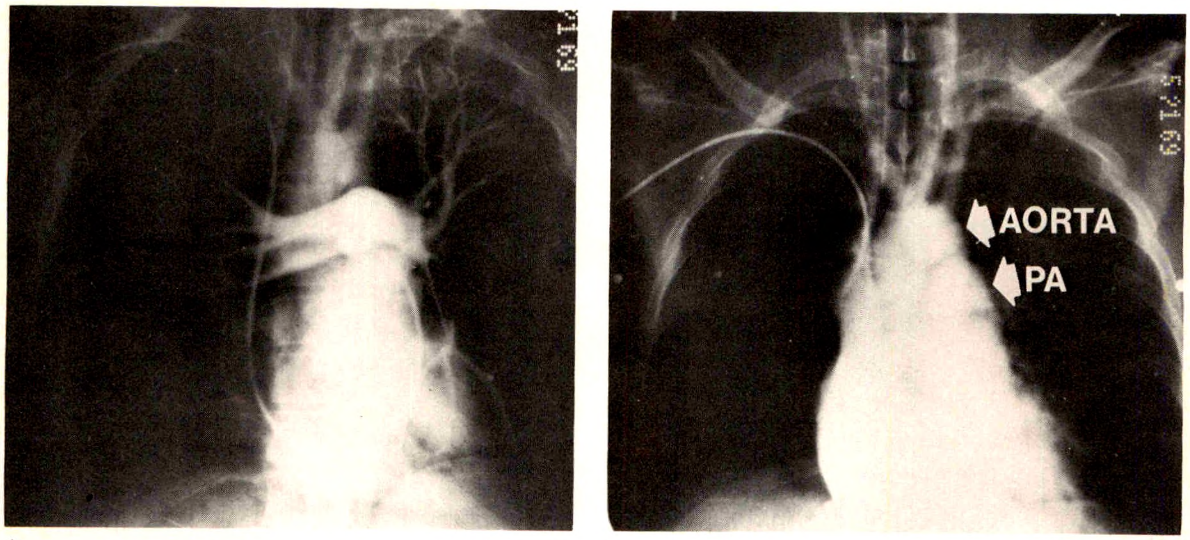
filling. Central venous pressure was 15 cm H_2O and Po_2 was 33 mm Hg breathing room air and 46 mm Hg with 40% oxygen. The patient's blood pressure was 140/80 mm Hg, and her electrocardiogram showed acute right heart strain.

Heart-lung bypass was instituted, and a 6 mm × 9.5 cm pulmonary embolus was extracted. A pencil-sized patent foramen ovale was closed with interrupted sutures. She recovered well from the operation but her cerebral status deteriorated, and she died three weeks later. Postmortem examination was not obtained.

It was our impression that this represented a poorer than expected course for a patient with a cerebral embolus, suggesting that her cerebral status had been worsened by cardiopulmonary bypass. There is confirmatory support for this premise in case reports by Padula [36], Wilson [49], and Gleysteen [16] and their associates: all their patients died from cerebral complications following embolectomy and inferior vena cava interruption.

Treatment

In endeavoring to outline a plan of therapy for pulmonary embolism, the clinician must consider the possibility of an intracardiac shunt. Usual clinical determinations take on new



A

B

Fig 2. (Patient 3.) (A) Pulmonary artery injection shows a large pulmonary embolus. (B) Superior vena cava injection shows simultaneous pulmonary artery (PA) *and aortic filling.*

meaning in this circumstance, and the decompressive effect of the shunt appears to provide little protection. The extent of anoxia is complicated by direct venoarterial perfusion through the shunt. The importance of right ventricular function is even more critical in patients with an intracardiac shunt, since it is the rise in right-sided pressure that makes these individuals particularly prone to paradoxical embolism. The right-sided pressure is influenced by the existence or nonexistence of prior cardiopulmonary disease [2] as well as the degree of embolic occlusion of the pulmonary arterial tree [8]. A patient with minor pulmonary embolization but with preexisting right ventricular hypertrophy and the potentially greater proportional increase in right-sided pressure is in danger of lethal paradoxical embolism.

The intent of the vena caval procedure in this set of circumstances is to prevent a paradoxical embolus. Interruption by ligation therefore would be preferable to one of the plication procedures. Many patients with elevated right ventricular pressure and in imminent failure are poor candidates for this procedure, however. When venous return is reduced, a precipitous fall in ventricular filling and myocardial contractility may ensue, with an irreversible fall in cardiac output [4, 14]. This has been our experience and is indirectly substantiated by a 50% mortality in a series of 34 patients with right ventricular failure [3]. Paradoxically, many are good-risk patients without prior cardiopulmonary disease and right ventricular hypertrophy. These individuals must be supported with heparin and oxygen until right-sided pressure drops, with experience indicating that this takes only several hours. One must also be prepared to assist ventilation and to ensure adequate circulating blood volume during the procedure and postoperatively. The use of a battery-powered, portable cardiopulmonary bypass unit may have a special place in this situation.

On the basis of our experience with pulmonary embolism diagnosed by pulmonary angiography over the past fifteen years and our special interest in the complication of paradoxical embolism, a plan of treatment is outlined. We recognize that every patient, because of inherent peculiarities, must be considered individually.

Heparin in adequate dosage is the primary therapeutic consideration in all cases. Operation is considered only if this drug cannot be used, if it fails as demonstrated by repeat angiography, or if there are extenuating circumstances such as an intracardiac shunt. We agree with Silver and Sabiston [41], McIntyre and Sasahara [30], and others that inferior vena caval procedures and pulmonary embolectomy are rarely indicated in this disease since heparin is so effective. Certainly, an operation should not be performed without pulmonary angiography and pressure determinations.

If the diagnosis of pulmonary embolism is being entertained, intravenous heparin therapy is started immediately. Control is maintained by repeated determinations of partial thromboplastin time and clotting time. In patients with significant embolism clinically, right heart catheterization is done with pressure recordings, and a pulmonary artery angiogram is performed. If emboli are demonstrated, a superior vena caval injection is done prior to removal of the catheter. This was suggested by Padula and Camishion [36]. If paradoxical embolus is suspected, a superior vena caval injection should always be done. This injection should be supplemented by a Valsalva maneuver or indicator-dilution technique [15, 32]. Hurley [24] has pointed out that the diagnosis of patent foramen ovale with right-to-left shunt should be suspected if radioactive material (technetium 99m albumin microspheres) is found in the kidneys at the time of lung scanning. If an intracardiac shunt is demonstrated, the patient should be considered for cardiopulmonary bypass with embolectomy and closure of the intracardiac shunt. This has been suggested previously by Gleysteen [16] and Lauten [27] and their colleagues as well as by the *British Medical Journal* [10].

The exception to the rule is the complication of cerebral involvement by a paradoxical embolus. Cardiopulmonary bypass, with its inherent requirement for high-dose anticoagulation, appears to further compromise the patient's cerebral status. If the mean pulmonary artery pressure is greater than 20 mm Hg, a Swan-Ganz monitoring catheter should be left in the pulmonary artery. When a pressure less then 20 mm Hg is obtained after a course of carefully administered heparin therapy, inferior vena caval interruption can be done following heparin reversal with protamine.

Patient 1 should have had an embolectomy and intracardiac shunt closure. His recovery on heparin alone was perhaps fortuitous and an unnecessary risk in an otherwise healthy young man. The case of Patient 2 was quite complex, but in retrospect he should have had a pulmonary embolectomy and not inferior vena cava ligation. Patients 3 and 4, because of cerebral infarction, should have had inferior vena cava ligation when pulmonary artery pressures were decreased.

In summary, although the statistical suspicion of the anatomical potential might be relatively small, the catastrophic nature of an eventual systemic embolus demands a crucial therapeutic decision. Paradoxical embolism should be included in the differential diagnosis of arterial embolism and entertained as a possible complication in all cases of pulmonary embolism. A diagnosis of intracardiac shunt can be made relatively simply by right atrial injection during right heart catheterization if right atrial pressure exceeds left, or by contrast dilution techniques with the Valsalva maneuver if right atrial pressure is normal. Finally, the presence of pulmonary embolism and intracardiac shunt presents a unique indication for surgical intervention.

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EDITORIAL

Role of the Blalock-Taussig Operation in the Hypoxic Infant with Tetralogy of Fallot

David C. Sabiston, Jr., M.D.

In 1944 Blalock performed the first systemic-pulmonary shunt for tetralogy of Fallot, and upon reflection today it is interesting to note that this historic procedure was performed on a child weighing only 4 kg [1]. The patient was severely ill, with frequent cyanotic spells leading to unconsciousness, and was greatly improved following a subclavian-pulmonary anastomosis. Since that time, thousands of Blalock-Taussig operations have been successfully performed with marked relief of symptoms. In the current issue of this journal (p 235), Chopra and associates review a series of 17 severely ill young children, 7 of them under 1 year of age, who underwent Blalock-Taussig shunts without any operative mortality. They emphasize meticulous technique, the advantages of *spatulation* of the end of the subclavian artery to permit a larger anastomosis, and the use of heparin intraoperatively. The excellent results in this series prompted the authors to conclude that it is the procedure of choice for the hypoxic infant with tetralogy.

Most agree that an anastomosis of the descending aorta to the left pulmonary artery (Potts procedure) is only rarely indicated, due primarily to the subsequent increase in the diameter of the anastomosis, the development of pulmonary hypertension, and the difficulty encountered in closure of this shunt at the time of the corrective operation. Of the 340 operations performed by Potts, the operative mortality was 9% with an additional late mortality of 20% [2]. While an ascending aorta–right pulmonary artery anastomosis (Waterston procedure) has been employed frequently, it is currently less popular due to recognition that it may be followed by kinking and distortion of the right pulmonary artery, creating potential problems at the time of correction [3].

During the past several years, the wisdom of a preliminary systemic-pulmonary shunt has been questioned by those who believe that an initial corrective procedure should be performed in nearly all infants requiring early operation [4–6]. Several series have been reported with a low operative mortality and encouraging postoperative results. Those who favor the corrective approach as the initial operation maintain that infants with documented hypoxic spells, severe hypoxemia, or suprasystemic right ventricular pressure are candidates for immediate correction, irrespective of age. It is emphasized that the intracardiac anatomy must be unambiguous on angiography and that contraindications to early correction include pulmonary atresia, hypoplastic distal pulmonary arteries, or origin of the anterior descending coronary artery from the right coronary artery. It is generally recognized that a high incidence of severe hypoplasia of the subpulmonary conus and pulmonary annulus will be present in such infants, being expressed by severe clinical symptoms which require early operative relief. Therefore, the need for placement of a large outflow patch is common, and it is frequently necessary to extend the patch across the valve ring to the pulmonary artery.

Despite the highly favorable results reported with early correction, others have seriously questioned this approach, believing rather that the Blalock-Taussig shunt should be performed first. It is their view that the mortality in general with initial correction is usually higher than that reported in the best series, and that the overall results are better if a shunt is the primary procedure. Thus, a series of 18 consecutive patients aged 3 to 30 months is reported without any operative mortality and with long-term patency of the anastomoses in all patients [9]. Moreover, concern has been expressed about the ultimate anatomical result in patients whose corrective procedures are performed early in life, the fear being that some will require an additional cor-

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From the Department of Surgery, Duke University Medical Center, Durham, NC 27710.

rective procedure due to the small size of the heart at the time of the original correction.

While most authorities agree that the vast majority of patients who undergo a palliative procedure will later require total correction, nevertheless it should be remembered that, in a long-term evaluation of the original Johns Hopkins series 15 or more years after an initial Blalock-Taussig shunt, 313 patients were still living with their first anastomosis *alone*. Of these, 125 women and 95 men had married and had a total of 196 children [7]. Indeed, Taussig reported 24-year follow-up of a patient who had undergone a subclavian-pulmonary anastomosis at the age of 23 months for severe symptoms and who was asymptomatic at the time of the report without any further operative procedure [8].

It is clear that opinion is divided at present concerning the procedure of choice in infants whose symptoms necessitate early operation for tetralogy of Fallot, with excellent series in the literature following either immediate correction or an initial subclavian-pulmonary anastomosis. Further observation and additional time will be required to elucidate this point before a uniform view becomes possible.

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Sudden Death and Coronary Heart Disease

By Sidney Goldstein, M.D.
Futura Publishing Company, New York, 1974
224 pp, illustrated, $15.00

Reviewed by William E. Neville, M.D.

For those interested in sudden death and associated coronary artery disease, this is an interesting and well-documented monograph. The author's excellent perusal of the literature, combined with his own experience at the Rochester General Hospital and as a visiting professor in Rotterdam, makes this a significant treatise. This is especially true because physicians and surgeons are growing more aware of the importance of sudden death and coronary disease in young individuals.

Oliver of Edinburgh, who wrote the foreword, aptly states that it should not be inevitable that young, productive individuals have to die suddenly. This is even more appropriate since enormous amounts of time and money are continually spent in efforts to treat the untreatable, repair the irreparable, and rehabilitate those who will never return to work. He readily recognizes that, although we appear to have reached an impasse in our present endeavors to prevent sudden death, this should be more of a challenge than a defeat. On the pessimistic side he states that at present we are unable to predict, on an individual basis, those who are likely to develop an acute heart attack in the immediate future; all we can do is to group people crudely into different grades of risk. Even assuming that we are able to predict an acute heart attack, we are unable to differentiate those who will develop a fatal ventricular arrhythmia during the course of it from those who will not have such a complication. Finally, he believes that there is no therapeutic procedure currently available to improve survival during an acute heart attack.

At the outset, the monograph reviews the history of sudden death and coronary artery disease and points out that 2,000 years ago Hippocrates recognized an association between chest pains and sudden death. However, little progress was made until the early 1900s, when attention was focused on acute myocardial infarction, and the importance of sudden death was really not brought into focus until the mid 1960s. The author reiterates that up to now efforts have been directed toward controlling arrhythmias, manipulating risk factors, and improving coronary circulation surgically. However, each of these factors is directed at a manifestation of myocardial ischemia and does not focus on the primary etiology of sudden death.

The book reads easily and the data are well researched. The content ranges over a wide variety of factors intermittently entangled in sudden death. Although this monograph is directed more along medical lines, there is a chapter on surgical and electrical prevention of sudden death that piqued my interest. The author aptly points out that although bypass surgery is seemingly well established at the present time, a major problem is that the patients who are most susceptible to sudden death on the basis of pathological and angiographic data are those with the most extensive coronary arterial disease—thus the individuals with the highest intraoperative mortality and greatest incidence of unsuccessful procedures. Although the number of patients with operable coronary artery disease who will die suddenly is not known, it appears that sudden death occurs predominantly in patients with extensive disease who may not be inoperable but who have two- or three-vessel involvement, which technically represents the most difficult surgical task. Despite this, he has great expectations for the success of coronary artery surgery in preventing sudden death. This should attract the attention of any surgeon wishing to have an excellent treatise in his library concerning this interesting and mysterious entity.

Newark, NJ

Emergency Care: Assessment and Intervention

Edited by Carmen Warner Sproul, M.D.,
and Patrick J. Mullaney, M.D.
The C. V. Mosby Company, St. Louis, 1974
406 pp, illustrated, $12.50

Reviewed by Watts R. Webb, M.D.

This book attempts to meet the need for a comprehensive textbook on emergency care that is applicable in a wide variety of settings and for personnel of diverse educational backgrounds and experience. It encourages continuing education and the interdisciplinary approach of physicians, nurses, and other allied health professionals, including firemen, policemen, and emergency medical technicians. The goal of presenting a guide for personnel of varied backgrounds makes maintenance of a standard educational level very difficult, and this is the major criticism of the book.

The contributors include primarily members of the medical and nursing staffs at the University of California, San Diego, School of Medicine. The content of the book includes the philosophy of emergency medical care, behavioral responses, legal considerations, psychiatric emergencies, and emergency diagnosis and care covering all systems of the body. This wide scope makes for superficial—and somewhat cookbook—coverage of most areas.

Most of the chapters are well written. However, there is a tremendous variance in the technical level of presentation from chapter to chapter and within several of the chapters. The chapter on legal considerations is very difficult to understand in terms of both style and content, though it does contain many helpful concepts. The chapter on behavioral responses of patients and staff in the emergency room is apparently unique to this book and is certainly very thoughtful and helpful.

The book appears to make a positive contribution to the guidance and training of allied emergency health personnel working within hospital emergency rooms. It seems to be oriented toward those emergency personnel who have had a background at least approaching that of the registered nurse. It is doubtful that the emergency medical technician stationed outside an emergency room or a policeman or fireman with more rudimentary training could profit materially from the book. Medical students could find it useful after having had physical diagnosis and their introductory courses in clinical medicine. For most topics it does not have the depth of coverage to serve as a text or as a guide for house officers or emergency room physicians, though they will profit from specific chapters.

Syracuse, NY

How to Live with Your Heart

Edited by Arthur Vineberg, M.D.
The New York Times Book Company, New York, 1975
219 pp, illustrated, $8.95

Reviewed by Derward Lepley, Jr., M.D.

This book by one of the world's best known pioneers in coronary artery disease is outstanding. It should be of extreme value to the patient who develops coronary occlusion and to the members of that patient's family, particularly the spouse. The explanations and answers to many questions that patients present to us after they have had a myocardial infarction or developed angina pectoris are very complete. Reading this book, an adult patient who has to change his life pattern rather abruptly gets very sound advice on extremely important areas of exercise, diet, smoking, and how the disease can be treated. The technical areas are well explained by Dr. Vineberg, but as with most texts, the advancement of the art is faster than publishing so that some areas are not up to date or are obsolete. A particularly good portion of this book is the explanation of diet and the very adequate charts of food calorie and cholesterol content along with weight charts.

This is an extremely valuable book for paramedical people working with patients who have coronary heart disease as well as for the patient himself and his family.

Milwaukee, WI

PROGRAM
FOR TWENTY-THIRD ANNUAL MEETING
OF THE SOUTHERN THORACIC SURGICAL ASSOCIATION

November 4–6, 1976
Princess Hotel, Acapulco, Mexico

November 4, 1976 (Thursday)

1:00 1. Surgical Management of Traumatic Intracardiac Injuries
Arthur C. Beall, Jr., M.D., Kenneth L. Mattox, M.D., Hartwell H. Whisennand, M.D., and Rafael Espada, M.D., Houston, TX

2. Subxiphoid Pericardial Window in Patients with Suspected Traumatic Tamponade
Kit V. Arom, M.D., J. David Richardson, M.D., Frederick L. Grover, M.D., and J. Kent Trinkle, M.D., San Antonio, TX

3. Congenital and Acquired Subclavian Steal Syndrome in the Pediatric Age Group
F. M. Midgley, M.D., and J. E. McClenathan, M.D., Washington, DC

4. Purulent Pericarditis in Infants due to *Hemophilus influenzae:* Diagnostic and Surgical Considerations
R. Nathan Grantham, M.D., Robert E. Hudson, M.D., Jerry D. Razook, M.D., E. F. Luckstead, M.D., W. M. Thompson, Jr., M.D., Ronald C. Elkins, M.D., and G. Rainey Williams, M.D., Oklahoma City, OK

5. Prospective Study of the Robertshaw Endobronchial Catheter in Thoracic Surgery
Raymond C. Read, M.D., Cheryl D. Friday, M.D., Carol N. Eason, M.D., and Gilbert Campbell, M.D., Little Rock, AR

3:00 6. Hiatus Hernia and the Respiratory Tract
Thomas L. Lomasney, M.D., Knoxville, TN

7. Repair of Pectus Excavatum in Children under Three Years of Age
Judson G. Randolph, M.D., William P. Tunell, M.D., and Duncan Morton, Jr., M.D., Washington, DC

8. Bronchogenic Cysts: Problems in Diagnosis and Management
Olyn M. Walker, M.D., George L. Zumbro, M.D., and Robert L. Treasure, M.D., Fort Sam Houston, TX

9. Eventration of the Diaphragm in Infancy and Childhood
Panagiotis N. Symbas, M.D., William J. Waldo, M.D., and Charles R. Hatcher, Jr., M.D., Atlanta, GA

10. Contemporary Management of Myasthenia Gravis: The Clinical Role of Thymectomy
Scott L. Faulkner, M.D., Abdolreza Ehyai, M.D., R. Darryl Fisher, M.D., Gerald M. Fenichel, M.D., and Harvey W. Bender, Jr., M.D., Nashville, TN

November 5, 1976 (Friday)
Morning Scientific Session

8:30 11. Prevention of Atelectasis following Cardiac Surgery: A Comparative Study of IPPB, the Incentive Spirometer, and Blow Bottles
Leigh I. G. Iverson, M.D., Roger R. Ecker, M.D., Harold E. Fox, M.D., and Ivan A. May, M.D., Oakland, CA

12. Bone Scanning in the Evaluation of Patients with Lung Cancer
Antonio T. Donato, M.D., E. Gifford Ammerman, M.D., and Otoniel Sullesta, M.D., Roanoke, VA

13. False-Positive Cytological Diagnosis of Lung Carcinoma in Patients with Pulmonary Infarction
William G. Scoggins, M.D., Rodney H. Smith, M.D., William J. Frable, M.D., Walter J. O'Donohue, Jr., M.D., James W. Brooks, M.D., and Lazar J. Greenfield, M.D., Richmond, VA

14. Perforations and Ruptures of the Esophagus: Report of 54 Cases—the Place of Conservative Management
William S. Lyons, M.D., Joseph W. Peabody, Jr., M.D., Vicente C. deGuzman, M.D., and Michael G. Seremetis, M.D., Washington, DC

15. Esophageal Replacement for Benign Disease: Indications and Treatment
Mark B. Orringer, M.D., Marvin M. Kirsh, M.D., and Herbert Sloan, M.D., Ann Arbor, MI

10:30 Presidential Address
James W. Brooks, M.D., Richmond, VA

11:15 Business Meeting

November 6, 1976 (Saturday)
Morning Scientific Session

8:30 16. The Assessment of Operability of Esophageal Carcinoma
Gordon F. Murray, M.D., Benson R. Wilcox, M.D., and Peter J. K. Starek, M.D., Chapel Hill, NC

17. Carcinoma of the Esophagus: Experience with a Philosophy for Palliation
John R. Hankins, M.D., Fred N. Cole, M.D., Safuh Attar, M.D., and Joseph S. McLaughlin, M.D., Baltimore, MD

18. The Use of the Heparin-Coated Shunt for Thoracic Aorta and Great Vessel Procedures: A Ten-Year Experience
James S. Donahoo, M.D., Robert K. Brawley, M.D., and Vincent L. Gott, M.D., Baltimore, MD

19. The Natural History of Long-Term Cardiac Pacing
William S. Stoney, M.D., Frederick E. Finger III, M.D., William C. Alford, Jr., M.D., George R. Burrus, M.D., Robert A. Frist, M.D., and Clarence S. Thomas, Jr., M.D., Nashville, TN

20. Ascending Aorta–Abdominal Aorta Bypass Graft: Indications, Technique, and Report of 10 Cases
Don C. Wukasch, M.D., Frank M. Sandiford, M.D., Gianantonio Nappi, M.D., George J. Reul, M.D., E. Ross Kyger III, M.D., Grady L. Hallman, M.D., and Denton A. Cooley, M.D., Houston, TX

10:30 21. A New Operation for Far-Advanced Cystic Medial Necrosis of the Aortic Root
Clarence S. Weldon, M.D., Robert C. McKnight, M.D., and Philip A. Ludbrook, M.D., St Louis, MO

22. Valve Replacement in Patients over the Age of 70 Years
Luis N. Bessone, M.D., Dennis F. Pupello, M.D., Richard H. Blank, M.D., Eric E. Harrison, M.D., and Sheldon Sbar, M.D., Tampa, FL

23. Coronary Venous Arterialization: Acute Hemodynamic, Metabolic, and Chronic Anatomical Observations
Joseph D. Marco, M.D., Hendrick B. Barner, M.D., Max Jellinek, Ph.D., John W. Standeven, Ph.D., and George C. Kaiser, M.D., St Louis, MO

24. Treatment of Severe Coronary Artery Disease with 5, 6, and 7 Saphenous Vein Bypasses: Review of 130 Consecutive Cases
Gerald F. Geisler, M.D., Maurice Adam, M.D., Ben F. Mitchel, M.D., Cary J. Lambert, M.D., and J. Peter Thiele, M.D., Dallas, TX

25. Prognostic Considerations in the Management of Ventricular Aneurysms
Donald C. Mullen, M.D., Roger P. Gabriel, P.A., Harjeet M. Singh, M.D., Robert J. Flemma, M.D., and Derward Lepley, Jr., M.D., Milwaukee, WI

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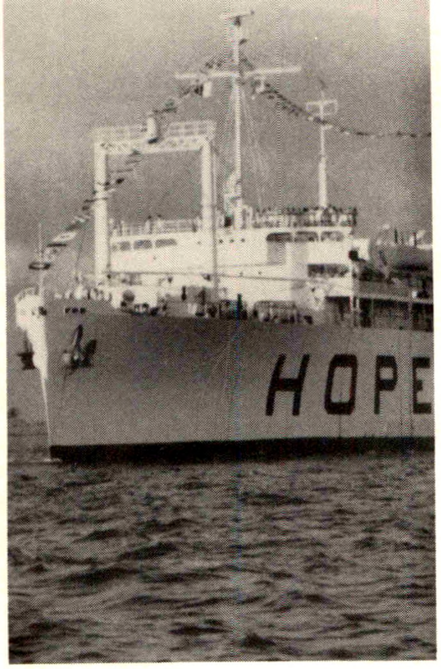

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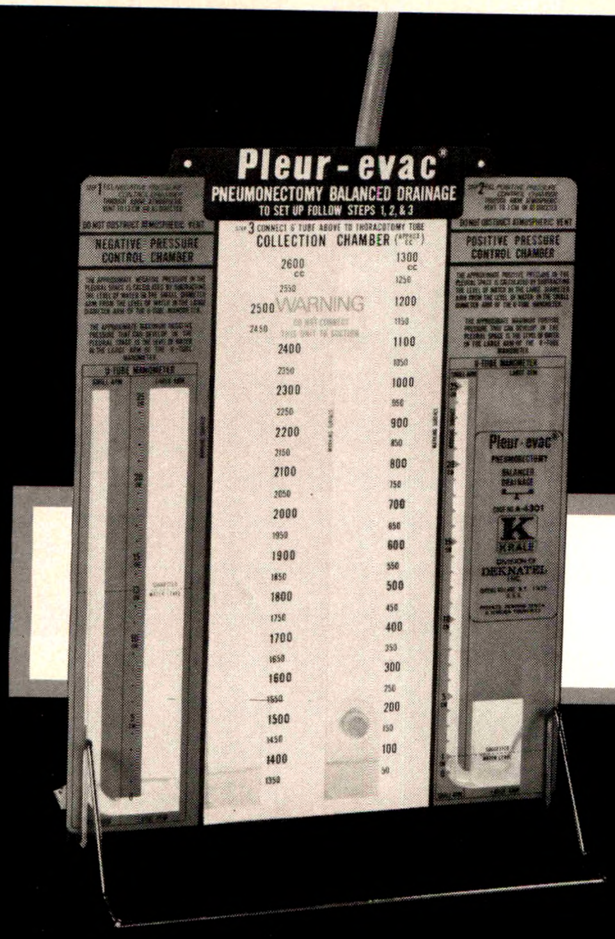
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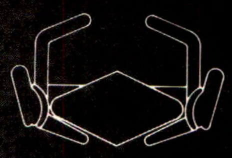

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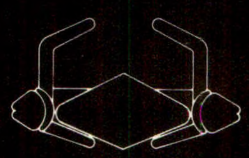

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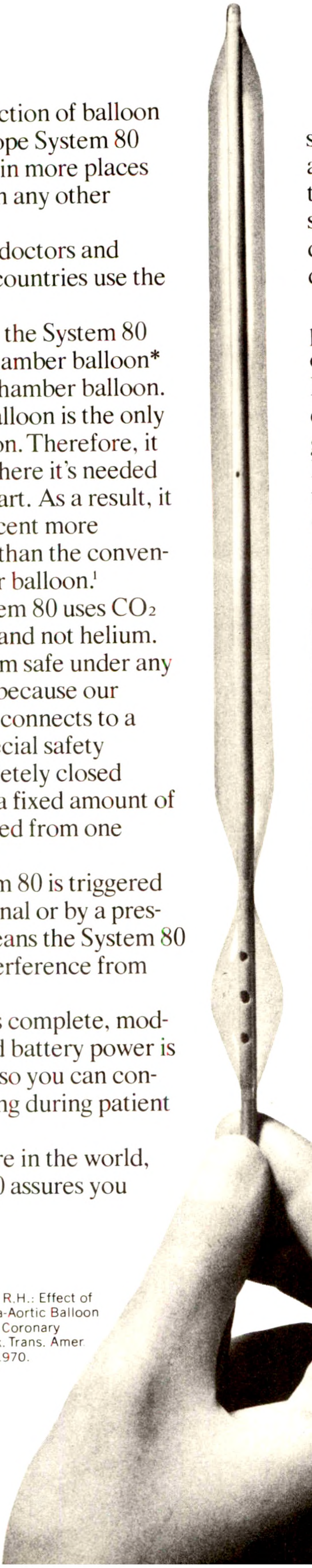

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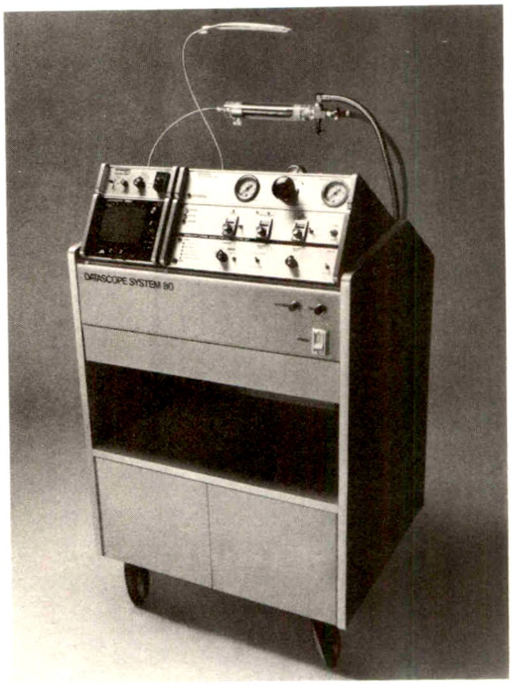

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[1] Bregman, D. Kripke, D.C., Goetz, R.H.: Effect of Synchronous Unidirectional Intra-Aortic Balloon Pumping on Hemodynamics and Coronary Blood Flow in Cardiogenic Shock. Trans. Amer Soc. Artif. Int. Organs, Vol. XVI, 1970.

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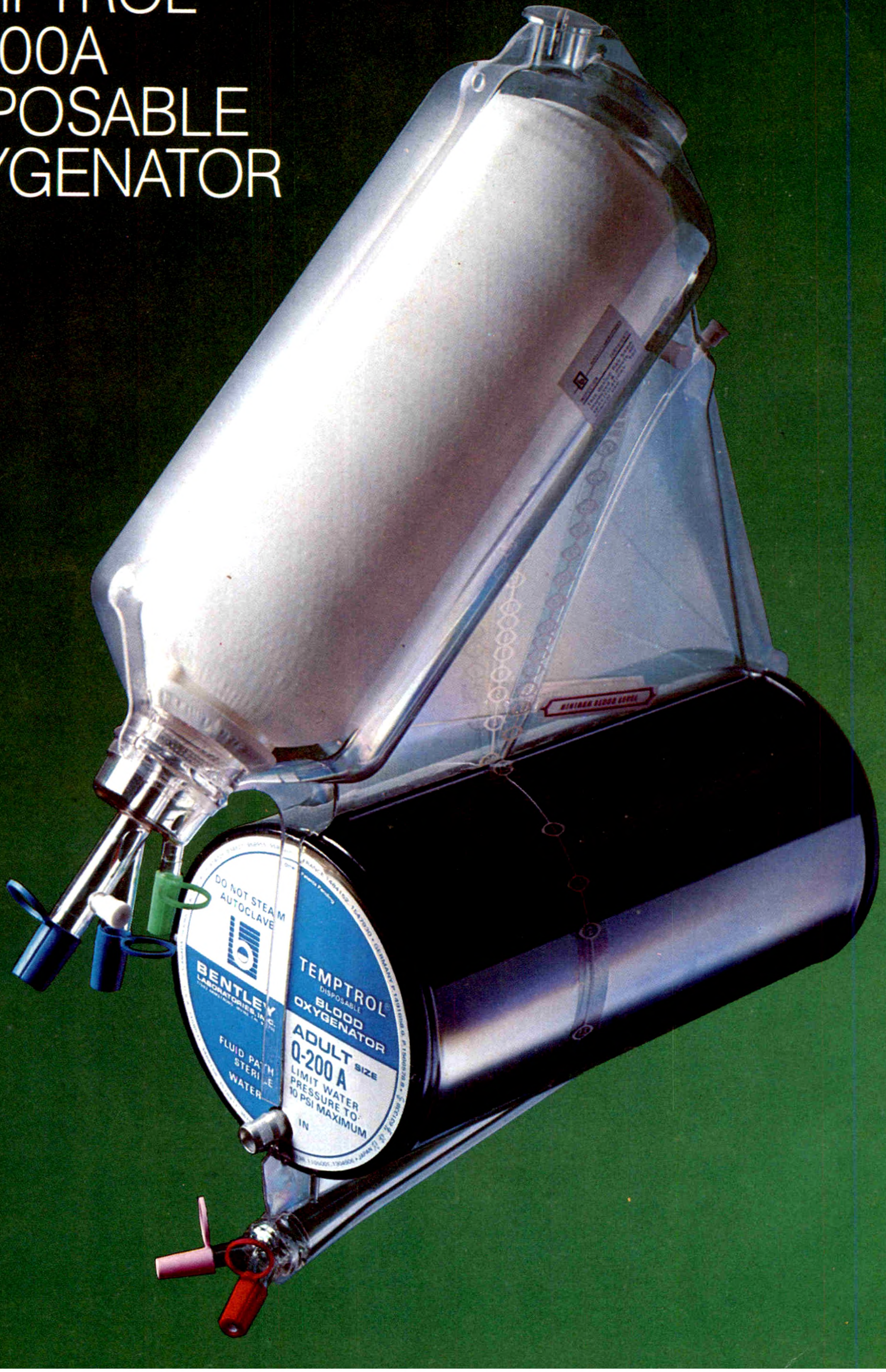

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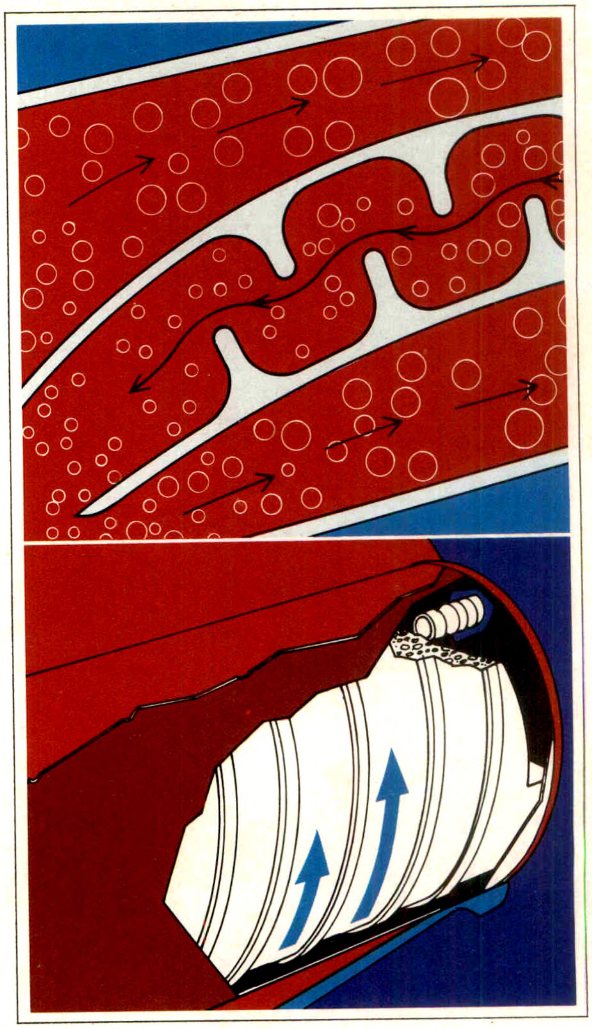

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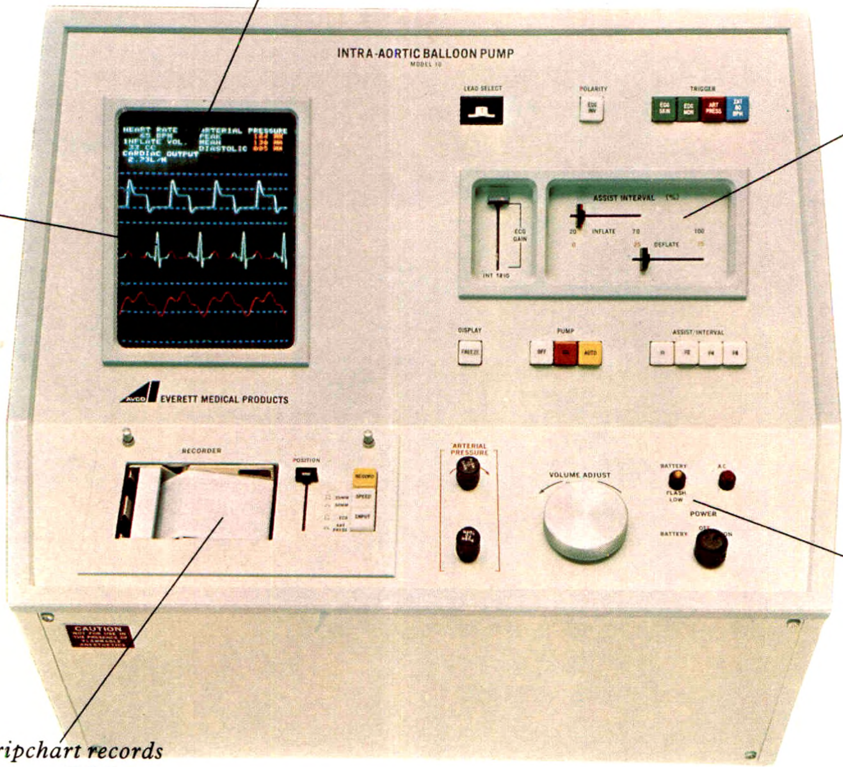

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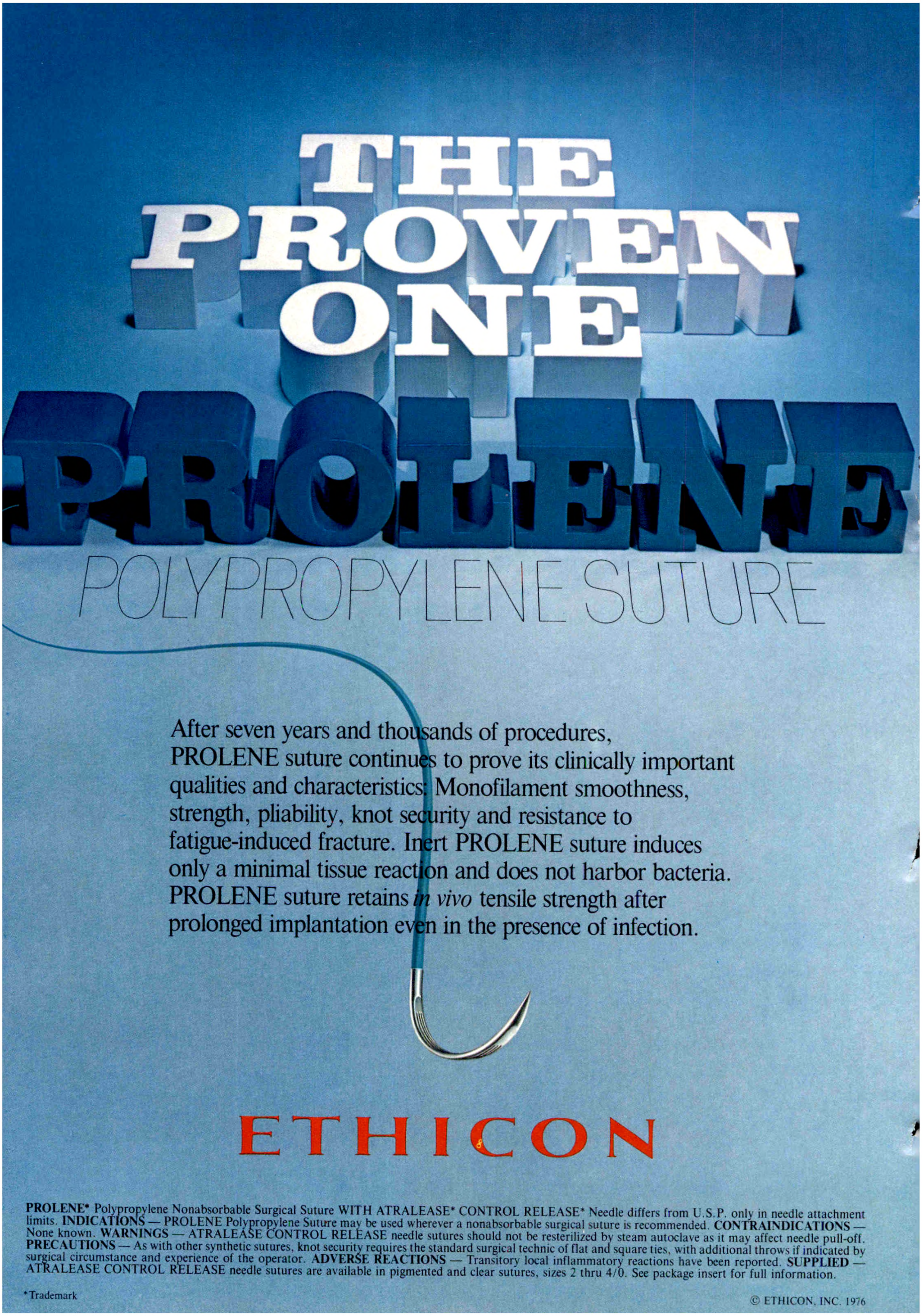

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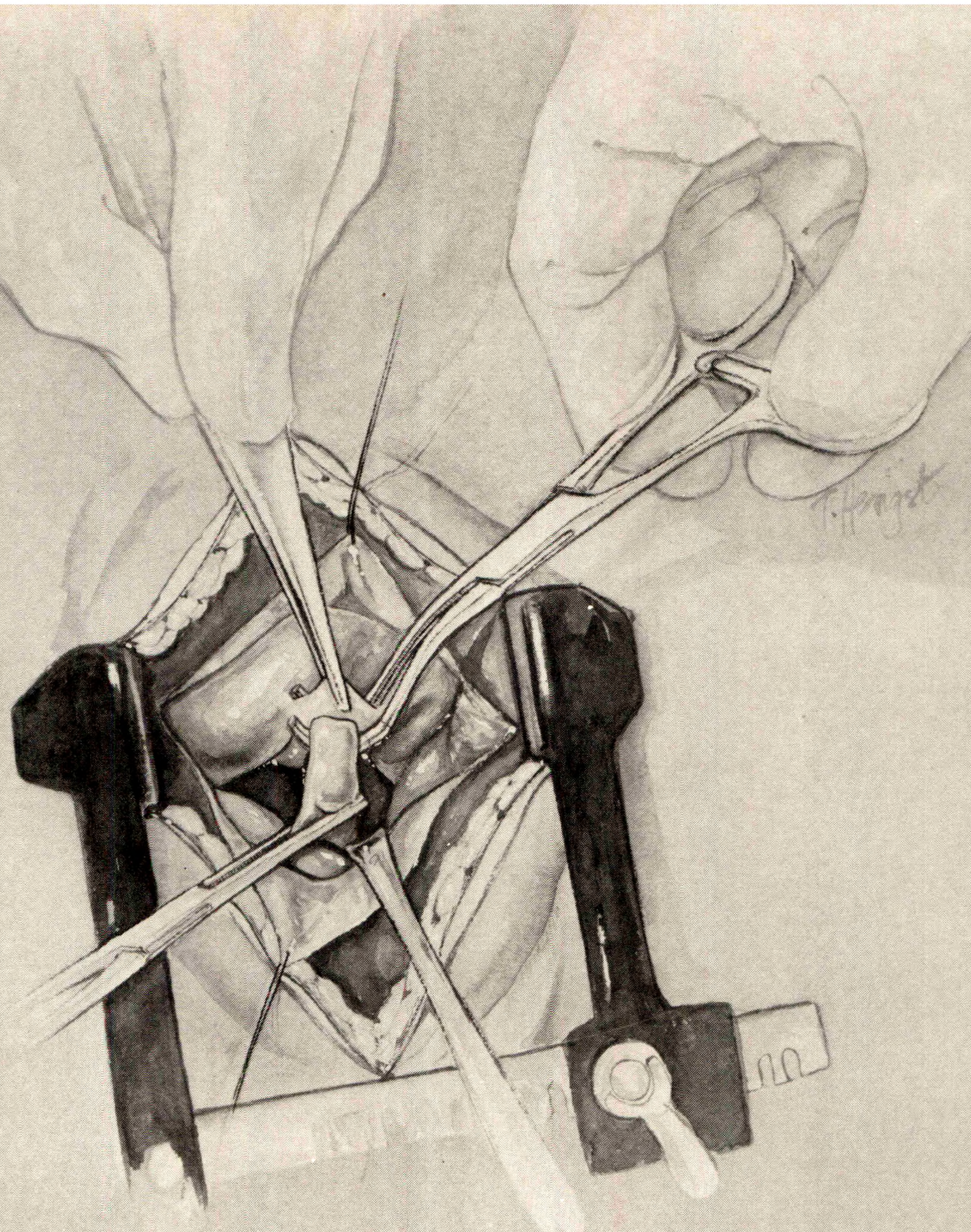

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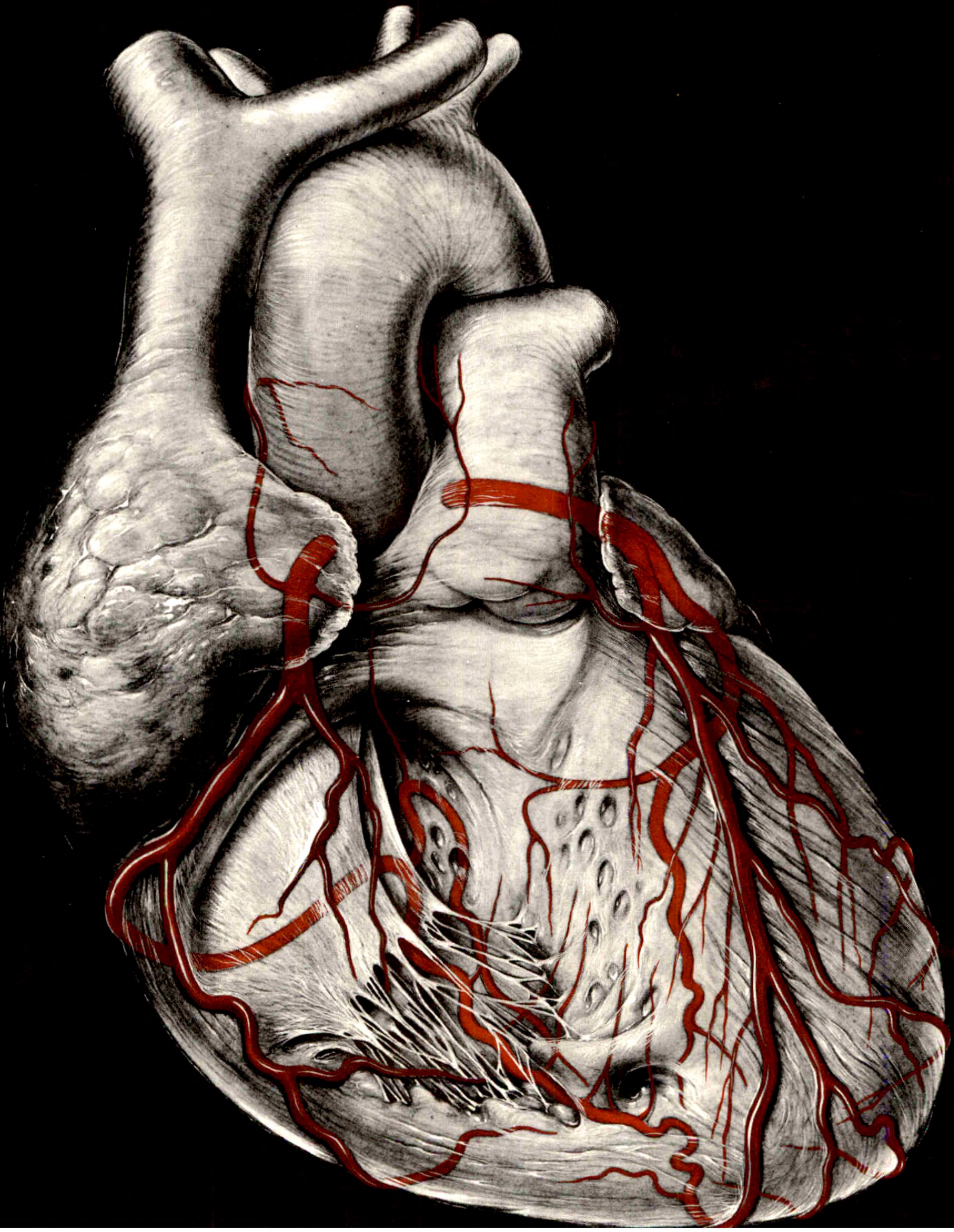

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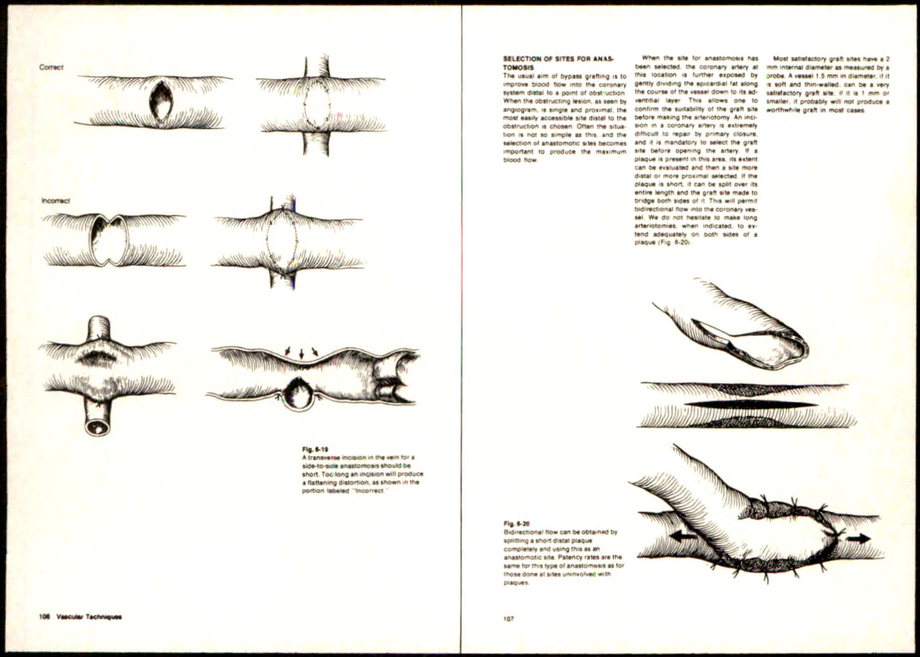

Fig. 6-19
A transverse incision in the vein for a side-to-side anastomosis should be short. Too long an incision will produce a flattening distortion, as shown in the portion labeled "Incorrect."

106 Vascular Techniques

SELECTION OF SITES FOR ANASTOMOSIS
The usual aim of bypass grafting is to improve blood flow into the coronary system distal to a point of obstruction. When the obstructing lesion, as seen by angiogram, is single and proximal, the most easily accessible site distal to the obstruction is chosen. Often the situation is not so simple as this, and the selection of anastomotic sites becomes important to produce the maximum blood flow.

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Most satisfactory graft sites have a 2 mm internal diameter as measured by a probe. A vessel 1.5 mm in diameter, if it is soft and thin-walled, can be a very satisfactory graft site; if it is 1 mm or smaller, it probably will not produce a worthwhile graft in most cases.

Fig. 6-20
Bidirectional flow can be obtained by splitting a short distal plaque completely and using this as an anastomotic site. Patency rates are the same for this type of anastomosis as for those done at sites uninvolved with plaques.

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THE ANNALS OF THORACIC SURGERY Vol 22 No 4 October 1976

ANNOUNCEMENT

We are pleased to announce the appointment of three new men to the Editorial Board of *The Annals of Thoracic Surgery*. They are: Richard E. Clark, M.D., Associate Professor of Surgery, Division of Cardiothoracic Surgery, Department of Surgery, Washington University School of Medicine, St Louis, MO; Anthony R. C. Dobell, M.D., Professor of Surgery and Director, Division of Cardiovascular and Thoracic Surgery, McGill University, and Surgeon-in-Chief, Montreal Children's Hospital, Montreal, Quebec, Canada; and E. Converse Peirce II, M.D., Henry Kaufmann Professor of Hyperbaric Surgery, Mount Sinai School of Medicine of The City University of New York, New York, NY.

Herbert Sloan, M.D.
Editor

The Compleat Thoracic Surgeon

Frederick H. Taylor, M.D.

The Southern Thoracic Surgical Association is unique in many ways. I know of no other surgical society with such a fine balance of full-time academic surgeons and private practitioners. Men from both areas participate in the scientific programs and in the administration of our association, and the Southern Thoracic is a happy mixture of these two groups. This is reflected by the fact that we give a President's Award for the best scientific paper presented at each meeting, and we also give the Osler Abbott and Tiki awards.

We must continue to promote our healthy combination of town and gown because we need each other. I suspect that the problems we face in the days ahead will be met only if we maintain our mutual respect for one another. Those of us in private practice should strongly support our teaching institutions. I call on all my fellow practitioners to give substantial annual financial support to both our graduate and undergraduate schools. I call on our teachers to seek out better ways for those of us in private practice to participate in continuing education. I believe better methods can be found than the present two- or three-day refresher courses. Would it be possible for practitioners as individuals or in small groups to go back to their teaching institutions for a week or so and actually observe and participate in the day-to-day management of patients? Could teachers come to community hospitals and actually show us how they manage surgical problems? Also, the Southern Thoracic might well consider using a half day or full day of its annual meeting for a postgraduate seminar devoted to one subject.

No doubt you have surmised from the spelling that I have borrowed my title from Izaak Walton's *The Compleat Angler* [21] and from Duke University's long-time Dean of Medicine, W. C. Davison, who wrote *The Compleat Pediatrician* [6] (Fig 1).

The Compleat Angler was first published in 1653. Piscator, the fisherman, in describing his art to Venator, the hunter, and Auceps, the falconer, said, "Angling is an art, and an art worth your learning: the question is rather, whether you be capable of learning it? For Angling is somewhat like Poetry, men are to be born so: I mean with inclinations to it, though both may be heightened by discourse and practice, but he that hopes to be a good Angler must not only bring an inquiring, searching, observing wit, but he must bring a large measure of hope and patience, and a love and propensity to the art itself" [21].

Dean Davison in the introduction to his book said, "In contrast to many pediatric books which too often resemble the old-fashioned hoopskirt in covering the subject without touching it, this book is like a G-string in touching the subject without any pretense of covering it, or even more aptly, like a brassiere in only touching the high spots" [6].

I approach my subject with great humility, because I realize that one man in one lifetime cannot adequately define or live up to being a compleat thoracic surgeon. Dr. Sam Stevenson, in his forthright fashion, put things in their proper perspective when he advised me to entitle this speech, "The Compleat Angler Who Thought He Was a Thoracic Surgeon."

Many years ago when I was accepted into medical school, the chairman of the admissions committee asked me what was wrong with one of my classmates who had made straight A's in undergraduate school. "Doesn't he do anything else besides study?" he wondered. Recently, I had occasion to call a dean about a young man who wanted to go to medical school. The Dean's very first question was, "Does he have all A's? Because if he does not, I doubt if he can get into medical school." A 180-degree change in course!

From the Department of Thoracic Surgery, Mercy, Presbyterian, and Memorial Hospitals, Charlotte, NC.

Presidential Address delivered at the Twenty-second Annual Meeting of the Southern Thoracic Surgical Association, New Orleans, LA, Nov 7, 1975.

Address reprint requests to Dr. Taylor, 1900 Randolph Rd, Charlotte, NC 28207.

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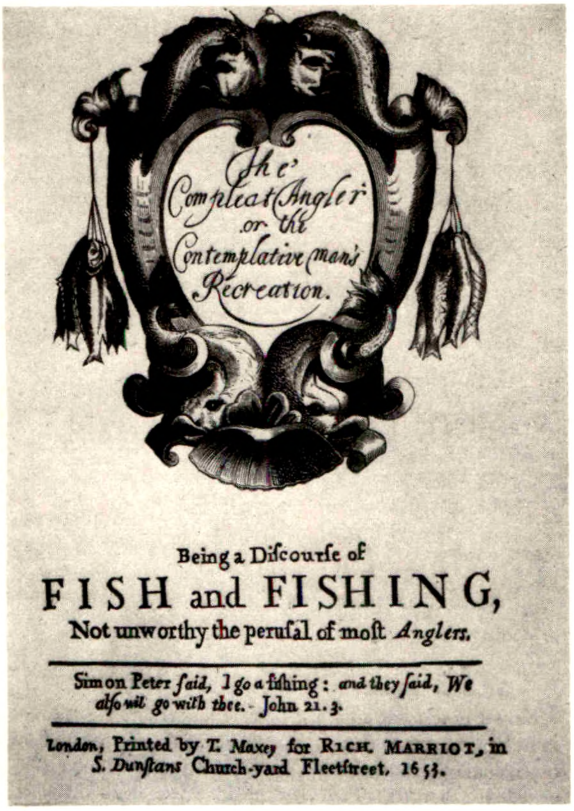

The Compleat Angler or the Contemplative man's Recreation.

Being a Diſcourſe of
FISH and FISHING,
Not unworthy the peruſal of moſt *Anglers*.

Simon Peter *ſaid, I go a fiſhing: and they ſaid, We alſo wil go with thee.* John 21.3.

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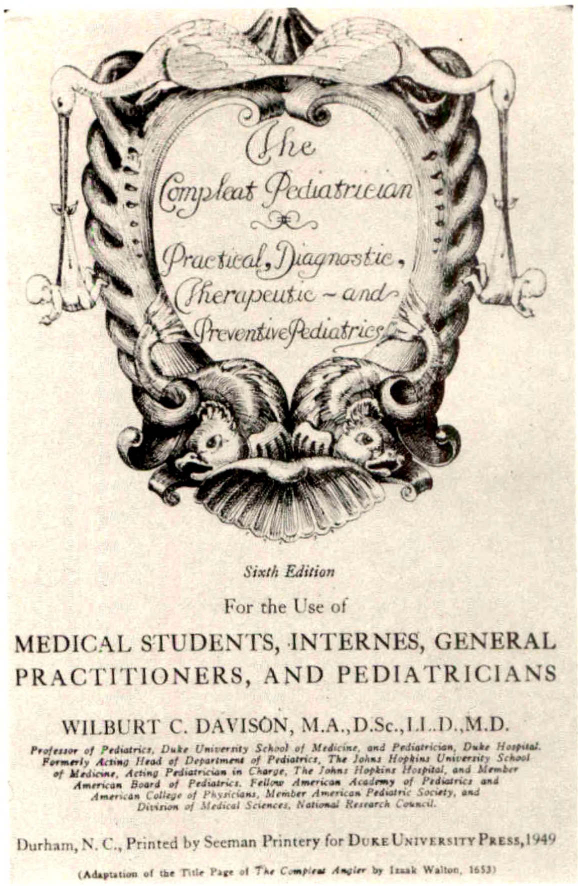

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Durham, N. C., Printed by Seeman Printery for DUKE UNIVERSITY PRESS, 1949

(Adaptation of the Title Page of *The Compleat Angler* by Izaak Walton, 1653)

Fig 1. Title pages from The Compleat Angler, *by Izaak Walton* [21], *and* The Compleat Pediatrician, *by W. C. Davison* [6] *(by permission of Duke University Press).*

I am not condemning the premium on excellence, but simply stating that excellence has many standards other than grades—desire, curiosity, the capacity for hard physical work, the willingness to refute fatigue and complete a job expertly no matter how late the hour. Good athletes with good minds should be looked over carefully. (It is interesting to note that Dr. Halsted introduced signal-calling to football when he played for Yale.)

I did not come here to criticize admissions committees, as I am very sympathetic with the enormous task they face in selecting proper candidates for admission to medical school. I do suggest, though, that the pendulum has swung too far in the emphasis on grades.

By our standards John Hunter (Fig 2) was a country bumpkin who would have difficulty finding a place in medical school today. He was described as "medical wildman and genius, body snatcher, frequenter of taverns and bordellos, a figure who might have been drawn by Hogarth . . ." and yet "this Scotsman's surgical skills were so imaginative and precise that he laid the foundation for modern practices—and his downfall" [16].

Sir James Mackenzie, the great Scottish cardiologist who first described atrial fibrillation, was a poor student. He could not understand why students were rewarded for memory rather than understanding. He left school at 15 years of age to enter an apothecary shop, where he worked for several years and then entered medical school at age 21 with an unimpressive academic record [18]. Today we see capable young men and women who have been turned down for medical school working as orderlies or laboratory assistants and trying to hang on until an opening in a medical school develops for them. These young persons deserve a second look.

Joseph Lister (Fig 3) received his college degree in 1847 without honors. Lister understood why John Hunter, his greatest hero, had pro-

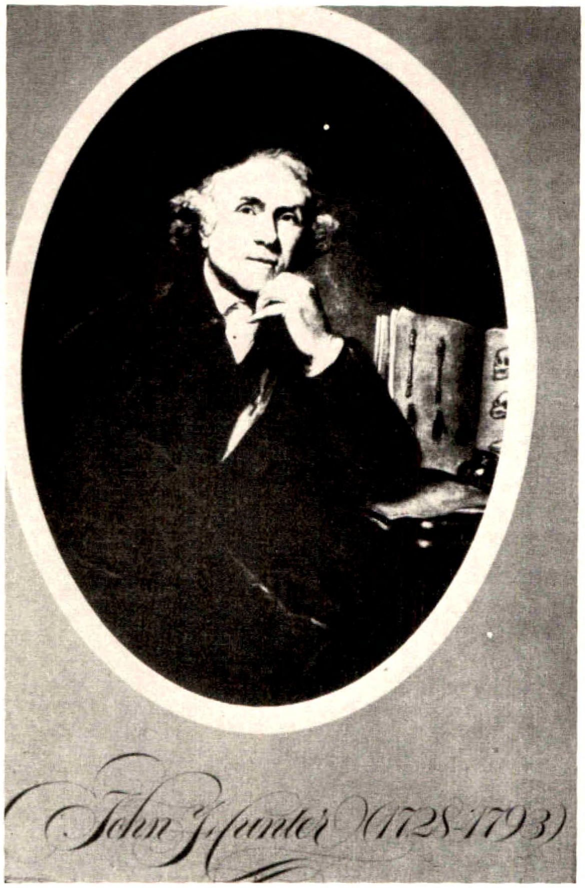

Fig 2. John Hunter. (Sir Joshua Reynolds's portrait hangs in The Royal College of Surgeons, London.)

Fig 3. Joseph Lister in 1869. (From R Truax: Joseph Lister: Father of Modern Surgery. *New York, Bobbs-Merrill, 1944.)*

tested against formal education—not entirely, as some people claimed, because he lacked it himself, but because he realized that it often prevented people from observing for themselves and frequently perpetuated mistakes which had been made in the past. It seemed incredible to Lister that physicians repeated Galen's mistake for 1,400 years [19]. Lister's achievements in antisepsis are well known to all of you. Lister also thought that catgut would be useful if the microbes in it could be killed. For twenty years he searched for the perfect absorbable ligature, an example of the perseverance which he hoped would make up for his lack of brilliance. You may be interested to know that Joseph Lister invented an aortic screw-clamp that saved a man bleeding from a large iliac aneurysm [19].

I submit that the good qualities of these "poor" students—imagination, the willingness to work in a pharmacy or a community hospital, and perseverance—should be searched for in any group of medical school applicants.

The Science of Surgery

In our field of practice we have seen a decline in emphasis on the art of surgery in favor of more so-called scientific modalities. Today we often see patients who have an obvious lung lesion on chest roentgenograms subjected to the expense of another day in the hospital because someone ordered laminagrams when the patient really needed bronchoscopy or resection of the lesion. A patient whose chest roentgenogram shows obvious pleural fluid is put through an extra day in the hospital so that lateral decubitus films can be taken. Simple percussion of the chest followed by needle aspiration of the fluid would obviate this expensive folly.

The computer is now a fact of life [9]. In 1972, 3,000 of the 8,000 hospitals in the United States owned, leased, or shared computers [5]. No doubt this figure is larger today. The computer has proved to be a useful servant in many areas, but it is an impossible monster when it becomes our master.

Computerized monitoring has its limited value, but it is disturbing to see a patient crucified to a bed with various attachments to flashing lights when he only needs to sit up and cough. Lay people in a community can be enticed into financing a computerized monitor at a cost of $100,000 or more. This takes some salesmanship, including stories about how many lives are being lost every year because of the lack of such a computer.

Some basic monitoring *is* necessary in the operating room. To this day, however, I place more trust in the anesthesiologist who is actually watching the patient's heart and lung movements than the one who is looking at nothing but his recording devices.

A new philosophy of pulmonary medicine has appeared on the scene in recent years. It brings forth great messages on IPPB, PEEP, arterial blood gases, and bedside or office transnasal bronchoscopy. I appreciate the need for these techniques and for the personnel trained in their use. In my opinion, however, IPPB can be justified only in cases of severe hypoventilation [3, 4, 14]. Many studies have shown that IPPB does not alter the incidence of postoperative atelectasis or pneumonia [4, 17], does not stimulate cough [17], and does not improve ventilation or blood gases [10]. Delivery of drugs to the bronchioles is no better with the expensive IPPB machinery than with a simple hand atomizer [4, 14], and the drying effect of IPPB far outweighs the moisturizing effect of any aerosol solutions used. The large number of people administering various materials through green tubes are also, on occasion, introducing microbes through cross-contamination [2, 4, 14].

We have repeatedly seen IPPB ordered routinely for all postoperative patients when what these patients need is an attentive doctor who will administer judicious nasotracheal suction. It is wrong to have thick secretions blown out into the alveoli by IPPB when the problem is easily solved by simple coughing. The cost of IPPB for a single patient may run into hundreds of dollars in a short period of time. Our hospitals' expenditures for oxygen have become enormous. Oliver Wendell Holmes once said, "Give us the luxuries of life and we will dispense with its necessities" [14].

We are indebted to Gustav Killian (Fig 4) for introducing the bronchoscope to us 77 years ago [11, 22]. Thoracic surgeons wrestled the rigid bronchoscope out of the hands of the ENT people some 30 years ago, and today we are confronted with pulmonary medicine people who are reporting the ease of bedside or office transnasal fiberoptic bronchoscopy. The occasional flooding of the tracheobronchial tree with blood or pus during bronchoscopy is neither appreciated nor provided for by this approach. The surgical implications of the bronchoscopic findings are not understood by most medical men. I trust all of you compleat thoracic surgeons will hang on to your bronchoscopes.

Doctors and nurses must return to the bedside and personally manage their patients. The foot of the bed is miles away from the side of the bed in the patient's mind, and the doctor's place is at the *side* of the bed, touching, looking at, speaking to, and yes, listening to his patient. Often one finds that a patient only needs to be detached from his equipment and urged to sit up in bed, to breathe deeply, and to cough with his chest being splinted by the surgeon's hands. Such direct action on our part will do more to encourage residents and nurses to follow suit than a ream of written orders on the patient's

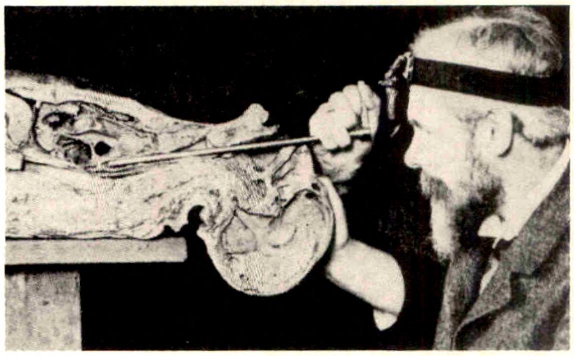

Fig 4. Gustav Killian, the first bronchoscopist, demonstrating his pioneer bronchoscope on a cadaver in 1898. (From F Zöllner: Gustav Killian: Father of bronchoscopy. Reprinted from the Archives of Otolaryngology, *82:656–659, 1965. Copyright 1965, American Medical Association.)*

chart. Even in this day of multiplying specialties and team approach, every patient needs *one* doctor who knows him and takes charge of his case. In our specialty this should be the operating surgeon.

The Art of Surgery

> *You should not cause shedding of blood in all practice of medicine. Nor cause any man injury by an iron instrument or by cautery.*
>
> Asaf (seventh century) [8]

Despite all our modern innovations, the art of surgery still revolves around the old triad of hemostasis, gentleness, and asepsis.

Surgery in sixteenth-century France was a despised profession. Ambroise Paré (Fig 5) did more than any other surgeon to raise its position to one of dignity and esteem. In 1552 this barber-surgeon first used the ligature in amputating a leg. He strongly condemned the prevailing method of using hot irons [15].

Fig 5. Ambroise Paré. (From Paré A: The Apologie and Treatise. *Edited by G Keynes. Chicago, The University of Chicago Press, 1952.)*

Today we see increasing use of the cautery not only for hemostasis, but also for actual incision across muscle masses. This practice is widespread among many fine surgeons. Most of them, however, learned their excellence of technique from master surgeons who used fine-pointed hemostats and fine ligatures for control of bleeding. Young residents brought up in the cautery method during their formative years are missing a great deal in perfecting the art of hemostasis.

One of earth's most precious natural resources is human blood. John Hunter once said to a contemporary, "Permit me to point out to you that you are a butcher, sir. The good Lord devised the circulatory system as an economical means of using the same blood over and over. I maintain, therefore, that when blooding a patient, this must be kept in mind. He has, after all, only so much blood to spare" [16].

There is much to be said in favor of conservation of blood during open-heart operations. Total hemodilution for cardiopulmonary bypass is successfully used by many of us. It obviates the hazards of transfusion reactions and serum hepatitis and probably improves the perfusion of tissues. The return of blood drawn preoperatively from the patient and reinfusion of his own blood remaining in the pump represent a great saving of this unique natural resource.

In the realm of gentleness, the name of Ambroise Paré again comes to mind. During his first campaign with the French infantry, Paré quickly realized that the accepted method of treating gunshot wounds with boiling oil did more harm than good. He substituted a more humane and less destructive dressing and soon established a reputation for skill in the treatment of wounds [15]—and yet today we see many surgeons who cauterize everything in sight.

Asepsis needs little comment other than to state that the coming of the antibiotic era and magic surgical soaps did not obviate the surgical precautions necessary to prevent infection. One wonders if present-day surgeons who think a one-minute scrub is adequate would have been happier in Lister's day, when surgeons considered personal cleanliness foppish and wore the same pus-encrusted gowns with pride, as this showed how busy they were. Lister, however, decided that cleanliness around wounds was desirable—a revolutionary idea in 1861. His work eventually did much to wipe out "hospitalism," as surgical infection was known in his day [19].

In recording the results of a surgical procedure we often fall into the trap of describing what we, the operating surgeons, think of the operation; seldom do we go into detail about what the patient thinks of it. The palliative operation for cancer immediately comes to my mind. Palliation should mean that the patient is better than he was the day *before* operation, rather than the day *after* operation. How often is this goal reached in the patient's mind after he undergoes a palliative operation for cancer of the lung or esophagus?

How often do we support our own feelings, rather than our patient's, when we send him off to the radiotherapist or chemotherapist for palliative treatment of his lung cancer? In 1807 Thomas Jefferson put it pretty well in a letter to Dr. Casper Wistar, professor of anatomy at the University of Pennsylvania, when he wrote, "To an unknown disease there cannot be a remedy. Here then the judicious, moral and human physician should stop" [1]. This, of course, is overstated, as we do have some success in the surgical treatment of cancer. We all know the usual signs of inoperability, but I suggest that the patient who is already ill with his cancer—who has the "gray look," as I call it—should be spared the ordeals of operation, irradiation, or chemotherapy.

Will and Ariel Durant in *The Lessons of History* said, "Our progress in science and technique has involved some tincture of evil with good. . . . We applaud the cures of modern medicine if they bring no side effects worse than the maladies. We are grateful for the added years that medical science gives us if they are not a burdensome prolongation of illness, disability, and gloom" [7].

The Future of Thoracic Surgery

Much work remains to be done. We may have become complacent about our present-day heart-lung machines, when in reality these machines still have some of the features of an eggbeater. The problems of blood trauma, of hemolysis, and of air, fibrin, or fat embolism are far from solved. We must search further for metabolic methods of patient protection during heart operations. Hibernation and hypothermia deserve more exploration.

We might look back on Sauerbruch's negative-pressure chamber as an overly complicated method of keeping the lungs expanded during chest operations [12, 13]. The solution, of course, lay in the development of the simple endotracheal tube.

Our heart-valve prostheses must be improved. The current cloth rags, metal, and plastic simply will not do. Our prosthetic arteries leave much to be desired. We need someone like John Hunter to strike out in imaginative directions to search for more biologically adaptable materials. Synthetic material which can be used for coronary artery bypass grafts or for relief of vein obstructions is yet to be discovered.

The problems of bleeding and clotting remain unsolved mysteries. We still do not understand the esophagogastric junction. Organ transplantation is in its infancy. The nonoperative solution for cancer, hypertension, and atherosclerosis remains to be found.

Our future is filled with social, legal, and political problems. Lawyers and politicians appear to be developing more influence than doctors in determining what we do, how we do it, and eventually how we will be compensated or punished [20]. Control of health care by these people seems to be developing through the process of turning to government to solve all health problems.

The oceans of the world support thousands of different creatures, each of which has made special adaptations and fits into the scheme of things. It would be ecological folly for any group to decide that only one species—the whale, the fish, the mollusk—should inhabit the seas, as this would lead to death of the environment. No PSRO, peer review, or other certifying or recertifying group should attempt to make all physicians conform to a common mold. As surely as the seas would die, original thinking and intellectual advances would perish. Let us beware of any group—professors, practitioners, lawyers, or government bureaucrats—who attempt to perpetuate only themselves. There is room for much flexibility in medical care. We of the Southern Thoracic must see to it that intellectual freedom is never weakened by individuals, special groups, or computers.

Surgeons, by nature, are men of action. Our activity sometimes leaves little time for contemplation. New ideas, however, come from contemplation. Izaak Walton said, "The very sitting by the river's side is not only the quietest and fittest place for contemplation but will invite an Angler to it. When God intended to reveal any future events or high notions to his prophets, he carried them either to the deserts or the seashore, that having so separated them from amidst the press of people and business, and the cares of the world, he might settle their minds in a quiet repose, and there make them fit for revelation" [21]. He also said that "action and contemplation meet together and do most properly belong to the most honest, ingenious, quiet, and harmless art of Angling" [21]. To this I would add that these two qualities, action and contemplation, do properly belong to the most honest and ingenious art of thoracic surgery.

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Recognition and Operative Management of Patients with Arteriosclerotic Coronary Artery Aneurysms

William C. Alford, Jr., M.D., William S. Stoney, M.D., George R. Burrus, M.D., Robert A. Frist, M.D., and Clarence S. Thomas, Jr., M.D.

ABSTRACT **Arteriosclerotic aneurysms of the coronary arteries have been noted in 38 patients undergoing cardiac surgical procedures. Age, sex, and risk factors are similar to those in other patients with coronary artery disease. A high incidence of previous myocardial infarction (24 of 38) is related to the frequency of clot formation and embolism associated with such aneurysms. There is also an increased risk of perioperative infarction following coronary artery bypass grafting if the suture line involves the aneurysm wall (6 of 6), but not when sutures are placed away from it. The importance of recognition and proper operative management is stressed.**

Arteriosclerotic aneurysms of the coronary arteries are being recognized with increasing frequency in patients having coronary cineangiograms. These aneurysms may be saccular or fusiform and have a diameter of at least twice that of the uninvolved vessel. They may involve one or more of the major coronary artery branches and may be single or multiple within any individual branch (Fig 1). Many of these people also have occlusive coronary artery disease and become candidates for coronary artery bypass grafting or related cardiac procedures. In the operating room, patients with arteriosclerotic coronary artery aneurysms frequently will have a more extensive arterial disease process and have been noted to have a higher incidence of perioperative myocardial infarction than those without aneurysms. To better understand this process, a review of 38 patients with such aneurysms undergoing cardiac operative procedures at our institution was undertaken.

From the Cardiac Surgical Service, St Thomas Hospital, and the Department of Thoracic and Cardiac Surgery, Vanderbilt University School of Medicine, Nashville, TN.

Presented at the Twelfth Annual Meeting of The Society of Thoracic Surgeons, Jan 26–28, 1976, Washington, DC.

Address reprint requests to Dr. Alford, Suite 501, St Thomas Medical Building, 4230 Harding Rd, Nashville, TN 37205.

Materials and Methods

Among 1,654 patients undergoing coronary artery bypass grafting at our hospital through March, 1975, 37 were noted to have coronary artery aneurysms on the coronary arteriogram. One additional patient undergoing mitral valve replacement for papillary muscle dysfunction was found to have an infarction secondary to a thrombosed coronary artery aneurysm at postmortem examination and is included in this study. Clinical observations included age, sex, history of previous myocardial infarction, and presence or absence of hypertension, obesity, diabetes mellitus, and hyperlipidemia. Prior myocardial infarction in a sibling or parent was also recorded.

Coronary cineangiograms were reviewed by at least two observers to determine the number of arteries containing aneurysms and their location. The operative record of each patient with an aneurysm was examined to determine the number of times a coronary artery bypass graft was performed to a vessel with an aneurysm and also the incidence of thrombus formation in such vessels. Perioperative infarction was diagnosed by the appearance of new Q waves in the early postoperative electrocardiogram.

Results

There were 38 patients in the study, 32 men and 6 women. Their ages ranged from 33 to 72 years, with a mean of 53.2 years. A summary of other clinical observations is shown in the Table. No pattern emerges from these data that could be used to distinguish these patients from others requiring coronary artery bypass. The frequency of prior myocardial infarction will be discussed subsequently.

Twenty-seven of the 38 patients had a bypass graft placed into a vessel with an aneurysm. In all 6 patients in whom the graft was sutured to

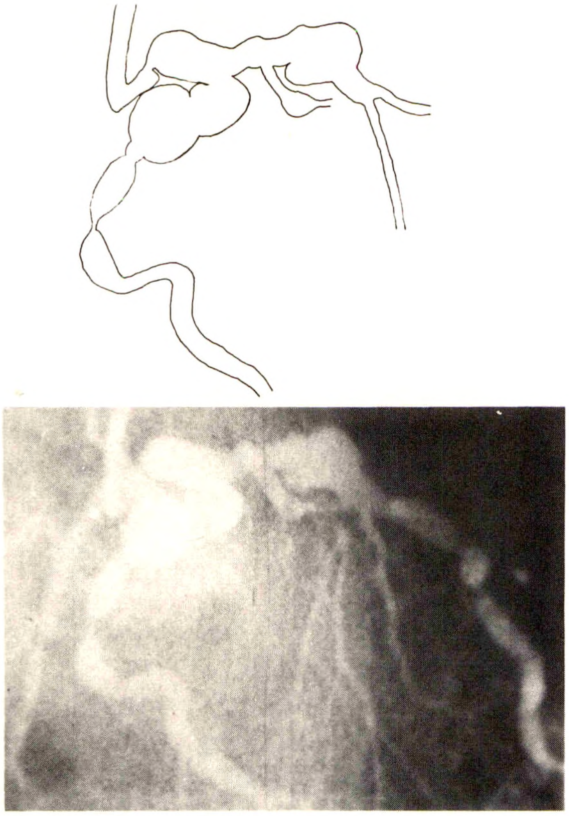

Fig 1. Aneurysms of the left coronary artery involving the proximal portion of the anterior descending and circumflex branches (right anterior oblique projection).

Risk Factors in 38 Patients with Coronary Artery Aneurysms

Risk Factor	No. of Patients	Percent
Previous myocardial infarction[a]	24	63
Hyperlipidemia[b]	20	52
Family history of myocardial infarction	16	42
Hypertension[c]	16	42
Obesity[d]	13	34
Established diabetes mellitus	7	18

[a] Documented by ECG or enzyme changes or both before arteriogram.

[b] Serum cholesterol >250 mg/100 ml; serum triglyceride level >190 mg/100 ml.

[c] Blood pressure > 90 mm Hg diastolic or > 140 mm Hg systolic or both.

[d] Body weight 20% greater than median ideal weight.

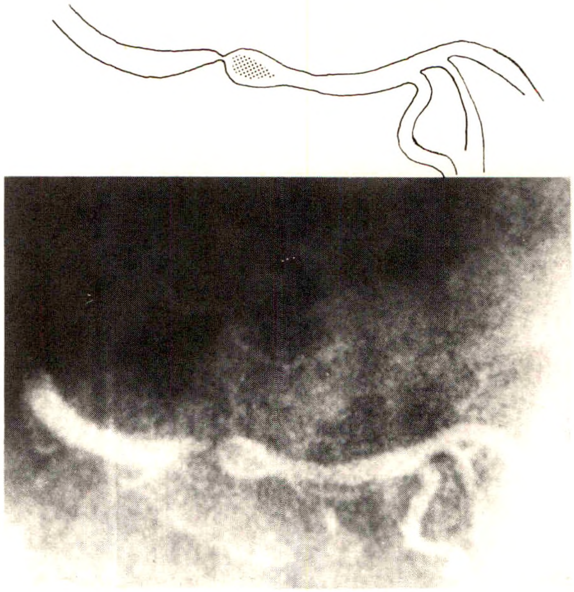

Fig 2. Aneurysm in midportion of the right coronary artery demonstrating intraluminal thrombus (right anterior oblique projection).

some portion of an aneurysm wall, nonfatal perioperative myocardial infarction resulted. No graft bypassed away from the aneurysm showed this complication. Nonocclusive thrombi were found in 5 aneurysms at the time of operation; in 1 this was noted preoperatively on the cineangiogram (Fig 2). In a sixth patient an occlusive thrombus was removed from an artery distal to the aneurysm and was thought to originate from it. A seventh patient who died following mitral valve replacement was found to have a massive myocardial infarction resulting from a thrombosed coronary artery aneurysm and causing mitral incompetence.

Seven of these patients had coronary artery aneurysms in all three major branches (circumflex, left anterior descending, and right). Seven had aneurysms in two major branches, and 24 had aneurysms in only one branch. Of this last group, 10 had multiple aneurysms in the single vessel. Nearly all involved the proximal to midportion of the coronary artery, with the distal portion of the vessel being relatively uninvolved.

Comment

Recognition and Incidence

A review article by Daoud and associates [3] in 1963 first delineated the prevalence of arteriosclerotic coronary artery aneurysms. They found 10 cases in 694 adults examined postmortem, for an incidence of 1.4%. The coronary arteries and in most instances the aorta showed advanced atherosclerosis. In 8 of the 10, death was directly related to abdominal aortic aneurysm. This latter relationship has not been supported subsequently in the literature. Only 2 of our patients had abdominal aortic aneurysms, both of which were successfully resected. Other reports of postmortem and clinical material have confirmed the atherosclerotic origin of most coronary artery aneurysms in adults [1, 3, 10, 13]. These patients demonstrate generalized arteriosclerotic coronary artery disease, often to a marked degree. When examined microscopically, the aneurysms show hyalinization and lipid deposits in the tunica intima, with focal calcification in some. Foreign body reaction around cholesterol crystals is present along with extensive destruction of the musculoelastic elements of the tunica media, resulting in thinning of this layer [3].

In view of the widespread incidence of coronary atherosclerosis and the tremendous increase in coronary cineangiography, it is surprising that more coronary artery aneurysms have not been reported. One problem has been a reticence on the part of the reporting physician to describe localized dilatations in coronary arteries as aneurysms. Alternate descriptive terms of what have been found to be true coronary artery aneurysms in this hospital include the following:

Spherically aneurysmatic vessel
Poststenotic dilatation
Ectasia
Patulous right coronary
Diffuse irregularity
Unusually dilated vessel
Link-sausage effect of coronary
Aneurysmal dilatations
Ectatic and irregular artery
Huge dilated artery
Ectatic and tortuous artery
Dilated luminal irregularities
Beaded artery
Large proximal vessel
Intermittent dilatation

A recent review has reported that 30 of 2,457 consecutive coronary arteriograms were interpreted as demonstrating "ectasia," an incidence of 1.2% [14]. Such terminology has tended to obscure the true frequency of this entity.

Causes of nonatherosclerotic coronary artery aneurysms in the adult include a congenital [1] or traumatic [13] origin, Takayasu's arteriopathy [6], mucocutaneous lymph node syndrome [11], periarteritis nodosa [9], or nonspecific inflammation [5]. All demonstrate a similar tendency toward thrombus formation and myocardial infarction.

Thrombosis and Infarction

A frequent finding within coronary artery aneurysms is the presence of organized thrombus material [3, 5, 13, 16, 20, 21]. These occasionally may be demonstrated by the coronary arteriogram. The clots may occupy all or part of the aneurysm lumen and can extend distally into the uninvolved coronary artery. The irregular internal surface and slow, turbulent flow of blood within the aneurysms predispose to thrombus formation [5]. We have noted clots in 6 of our 37 patients and in the 1 postmortem specimen, while Daoud reported clot in 6 of 10 aneurysms examined [3].

The high incidence of prior myocardial infarction in persons with all types of coronary artery aneurysms is thought to be related to this propensity to initiate thrombosis and subsequent embolism [5, 17, 19]. In the present series, 24 of 38 patients demonstrated prior myocardial infarction. In a group of 30 patients with so-called coronary artery ectasia there were 24 with old infarcts [14]. Other authors have also concluded that while coronary artery aneurysms rarely rupture, death is usually due to thrombosis of the aneurysms or related myocardial infarctions [15, 20].

Operative Considerations and Perioperative Infarction

A major impetus to this review of coronary artery aneurysms was an initial high incidence of perioperative myocardial infarction after bypass grafts were placed at the aneurysm site. In 6 patients in whom the vein graft was sutured to some portion of the aneurysm wall, nonfatal perioperative infarction resulted. It is assumed that the infarctions were the result of distal coronary embolism from the suture lines in these friable, diseased areas. Since we adopted a policy of suturing the graft beyond the aneurysm site, 20 patients have had such grafts placed with no resulting infarctions. In 1 of this latter group, the aneurysm was ligated distally as a prophylactic measure to prevent embolism. Routine ligation has been proposed [19, 20] but does not appear indicated from this series. The remaining 11 patients demonstrated aneurysms in coronary arteries not involved with occlusive lesions, and no operation was done to them. Rather, grafts were placed to other vessels with stenoses, and again no infarctions were noted.

In certain patients in whom the aneurysm is of a large size or rupture seems imminent, direct repair or removal can be done with a certain morbidity. Lateral aneurysmorrhaphy has been reported on 2 occasions [1, 2] with no infarctions. Excision of an aneurysm with reconstruction by interposed vein graft has also been reported twice [4, 5]; nonfatal infarction occurred in 1 of these. However, the risk of thrombosis and embolism is such that care is needed during coronary artery bypass to lessen the chance of operative infarction.

Conclusions

Arteriosclerotic coronary artery aneurysms are being recognized with greater frequency. The true incidence is unknown, but 0.5% [18] to 1.5% [14] of patients undergoing coronary cineangiograms for suspected ischemic disease will demonstrate this lesion. This report presents 38 such patients who have undergone cardiac surgical procedures. No significant pattern of risk factors allows this group to be suspected prior to angiography [8]. Twenty-four of 38 had at least one previous myocardial infarction. Many of the younger people had diffuse disease with multiple coronary artery aneurysms; they represented advanced atherosclerosis, but again without identifying risk patterns.

The pathogenesis of this lesion remains uncertain. Except for the traumatic and congenital variety, nonatherosclerotic coronary artery aneurysms seem to have an arteritis of the vasa vasorum related to their formation [3, 9, 11, 16, 18]. It can be postulated that the arteriosclerotic process may also involve the vasa vasorum before lipid deposits occur, resulting in degeneration of the media and weakness of the arterial wall, which then predisposes to dilatation in these areas.

Thrombosis is a very real hazard in people with coronary artery aneurysms. Distal embolism probably accounts for the frequency of myocardial infarctions in these patients and is cause for concern when undertaking an operation. Long-term anticoagulation therapy is a reasonable approach in the patient with a patent coronary artery aneurysm and has been recommended [16]; however, thrombosis has been reported in 1 aneurysm in spite of adequate anticoagulation therapy [11].

The possibility of the occurrence of coronary artery aneurysms in patients with atherosclerotic coronary artery disease should be kept in mind. With a proper approach to the operative management of these patients, significant clinical improvement in the ischemic condition should be possible. Follow-up data available at this time are insufficient to evaluate the long-term results of this lesion.

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Discussion

DR. REINOLD J. JONES (San Francisco, CA): I would like to congratulate Dr. Alford and his coauthors on their experience, and I appreciate their sending the manuscript to us for review before the meeting. Our experience at St. Mary's is similar to that of Dr. Alford. Among 713 of our patients 6 had coronary aneurysms. There were no intraoperative or postoperative deaths in this group, and no intraoperative or postoperative infarctions were found. As in Dr. Alford's group, all of the patients in our study also had a significant obstruction present or they had had infarction on an embolic basis preoperatively.

Cardiologists report a much higher incidence of aneurysms without any arterial obstruction on cineangiographic studies. These are not being referred for operation. Dr. Alford has given us a list of descriptive terms that are seen on cineangiography reports. These are not all true aneurysms, and I think the entity that is probably mistaken most frequently for an aneurysm is the poststenotic dilatation. This poses a problem to the surgeon.

We realize that most of the patients who have fusiform aneurysms can be observed. However, those who have a large saccular aneurysm such as described here and such as Dr. Alford has shown you predispose to turbulent flow; and, of course, the sequela of embolus is always possible. Should we therefore be considering these patients for prophylactic bypass procedures even though there is no significant obstruction distal to the aneurysm?

Dr. Alford has shown you that anastomosing the vein graft to the side of the aneurysm is to be avoided. All our patients had their aneurysms bypassed below the aneurysm site. We also consider it mandatory that the aneurysm be excluded from the area of flow. We do this simply by putting a hemoclip distal to the aneurysm and proximal, of course, to the vein bypass graft. This is done for two reasons: the first is that the embolic phenomenon that still could occur from the aneurysm is thereby obviated, and the second is, we believe that if we leave the aneurysm open without significant distal obstruction, competitive flow could possibly cause the graft to occlude.

DR. ALFORD: I thank Dr. Jones for discussing this paper. He has brought up some problems that I do not think I can answer definitely. One is, what is the difference between poststenotic dilatation and an atherosclerotic aneurysm? As I showed you in one of my figures, the dilatation beyond a stenosis which I ordinarily would call poststenotic did have thrombus in it, and on 2 occasions in which we sutured a graft to the poststenotic dilatation, we did get postoperative myocardial infarction. So since these areas look like they have arteriosclerotic involvement and since they act so much like the aneurysm, we elect to treat them all the same.

As far as the advisability of ligating all coronary artery aneurysms, I cannot say that is not a good thing. We probably will do more of it. In the patients with unligated aneurysms whom we followed, there has been 1 definite myocardial infarction which may have been the result of embolism from that aneurysm. It certainly makes us consider the procedure more often.

Retrograde Venous Cardiac Perfusion for Myocardial Revascularization: An Experimental Evaluation

G. Doyne Williams, M.D., Hugh F. Burnett, M.D.,
Bobby L. Derrick, M.D., and Charles H. Miller, M.D.

ABSTRACT **This study evaluates cardiac function in dogs during retrograde perfusion through the coronary sinus. Five hearts perfused retrograde in an ex vivo apparatus demonstrated rapid and marked increases in weight and perfusion pressure, became hemorrhagic, and contracted poorly within one hour. Five similarly perfused hearts treated with phenoxybenzamine experienced no increase in weight or perfusion pressure and maintained good color and contractions for up to one hour. Five additional hearts treated with phenoxybenzamine did not develop hemorrhage, edema, increased weight, or increased perfusion pressure but could maintain the systemic circulation for only brief periods after 15 minutes of intermittent cardiopulmonary bypass support.**

We conclude that cardiac viability can be maintained with retrograde perfusion enhanced with alpha blocking agents. However, hearts so perfused cannot maintain adequate systemic pressure. The data suggest that extensive myocardial revascularization through the retrograde venous route would be ineffective.

Arterialization of the coronary venous system as a means of revascularizing the diffusely atherosclerotic heart is an attractive concept. Patients are frequently seen with diffusely diseased coronary arteries which preclude conventional forms of aortocoronary or direct internal mammary–coronary artery grafts. While endarterectomy in conjunction with aortocoronary vein grafting allows partial revascularization in a small percentage of these patients, subsequent graft failure is frequent. Experimental and clinical interest has thus been stimulated to revascularize the ischemic myocardium by using the coronary venous system.

The present study seeks to evaluate the effectiveness of retrograde venous myocardial perfusion. Emphasis is placed upon the evaluation of hearts in which the total blood supply is introduced by means of the coronary sinus and in which the coronary arteries have been divided at their origin to provide a new route of venous drainage. The studies include both ex vivo isolated perfusion experiments as well as evaluation of in vivo retrograde perfusion of hearts supporting the systemic circulation.

Experimental Materials and Methods

Twenty dogs were divided into four groups of 5 animals each. Groups I and II underwent ex vivo retrograde perfusion and Groups III and IV underwent similar in vivo studies. Groups I and II were studied with the perfusion apparatus depicted in Figure 1.

Group I

These 5 hearts were placed in the apparatus shown in Figure 1. Oxygenated normothermic dog blood was infused into the cannulated coronary sinus with flow at 50 ml/min. The blood passed through the coronary veins, and a portion of it was collected for sampling purposes by means of cannulas in the right and left coronary artery ostia. The remaining blood entered the cardiac chambers and drained out the various openings in the heart into the funnel collection system for return to the pump oxygenator. The coronary sinus perfusion pressure, heart weight, and "arterial" and "venous" oxygen saturations were recorded for one hour. These data are recorded in Table 1 and appear in graph form in Figure 2.

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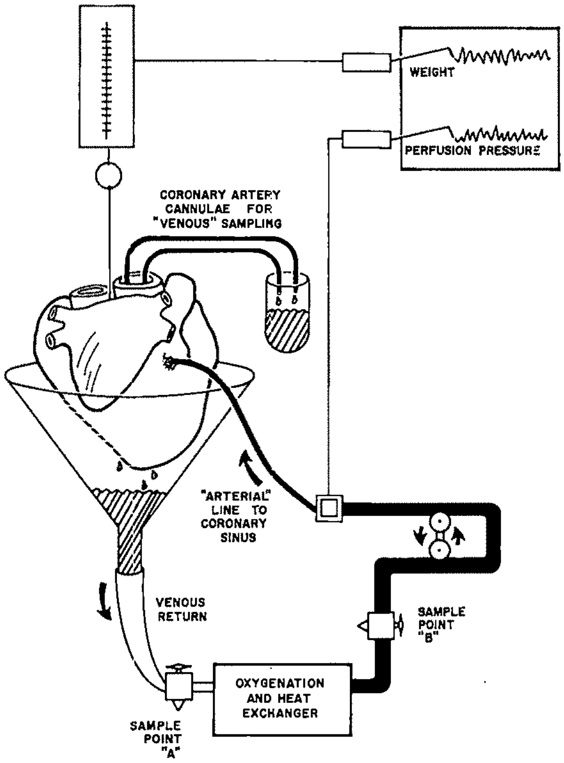

WEIGHT
PERFUSION PRESSURE
CORONARY ARTERY CANNULAE FOR "VENOUS" SAMPLING
"ARTERIAL" LINE TO CORONARY SINUS
VENOUS RETURN
SAMPLE POINT "B"
OXYGENATION AND HEAT EXCHANGER
SAMPLE POINT "A"

Fig 1. Ex vivo retrograde cardiac perfusion system used in Groups I and II.

Group II

An additional 5 hearts were perfused and monitored exactly as described for Group I except that phenoxybenzamine (1.0 mg) was added to the perfusate. The resulting data are listed in Table 1 and appear in graph form in Figure 2.

Group III—In Vivo Studies

Five animals were placed on cardiopulmonary bypass as shown in Figure 3. Venous return was obtained with a single right atrial cannula, and oxygenated blood was returned to the dog through the right femoral artery. The aorta was then cross-clamped and the heart was packed in ice slush while the right and left coronary arteries were encircled with a suture at their point of origin from the aorta. A human saphenous vein segment was sewn to the coronary sinus in an end-to-side manner to provide retrograde entry for perfusion. The coronary arteries were divided near their origin and individually cannulated to allow collection of the newly routed venous blood. The coronary sinus orifice was ligated to prevent reflux of blood into the right

Table 1. Ex Vivo Studies of Hearts Subjected to Retrograde Venous Perfusion for Myocardial Revascularization

Group & Study Method	Time (min)	Pressure (mm Hg)	Weight (% increase)	AV O_2 Diff. (% saturation)
Group I (controls without phenoxybenzamine)[a]	0	38.0 ± 2.7	100 ± 0	29.4 ± 5.2
	15	70.0 ± 28.9	188 ± 30.1	25.0 ± 8.1
	30	109.0 ± 50	257.6 ± 23	20.6 ± 1.9
	60	136.0 ± 29.7	323.4 ± 26.9	17.8 ± 5.7
Group II (hearts treated with phenoxybenzamine)[a]	0	33.4 ± 13.8	100 ± 0	35.8 ± 12.1
	15	37.8 ± 18.9	104 ± 5.1	43.4 ± 12.7
	30	39.8 ± 19.8	114.0 ± 9.6	45.4 ± 9.8
	60	42.8 ± 21.8	118.2 ± 12.9	47.8 ± 8.7
Groups I & II: statistical analysis (t-test)	0	$t = 0.73$	. . .	$t = 1.09$
	15	$t = 2.08$	$t = 6.15$ ($p < 0.001$)	$t = 2.73$ ($p < 0.05$)
	30	$t = 2.87$ ($p < 0.05$)	$t = 12.9$ ($p < 0.001$)	$t = 5.56$ ($p < 0.001$)
	60	$t = 5.6$ ($p < 0.001$)	$t = 15.4$ ($p < 0.001$)	$t = 6.44$ ($p < 0.001$)

[a] Mean of 5 hearts with one standard deviation.

AV = arteriovenous.

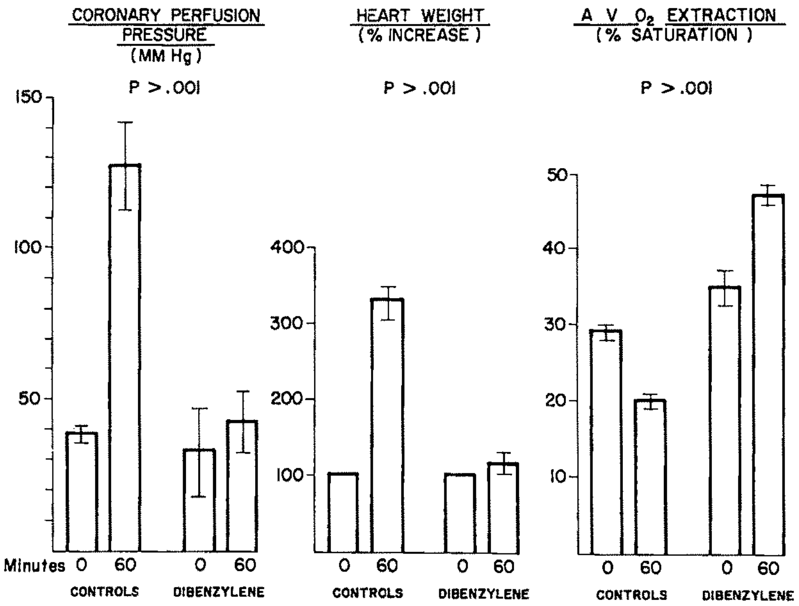


Fig 2. Comparison of ex vivo control hearts (Group I) with dibenzylene (phenoxybenzamine)-treated hearts (Group II).

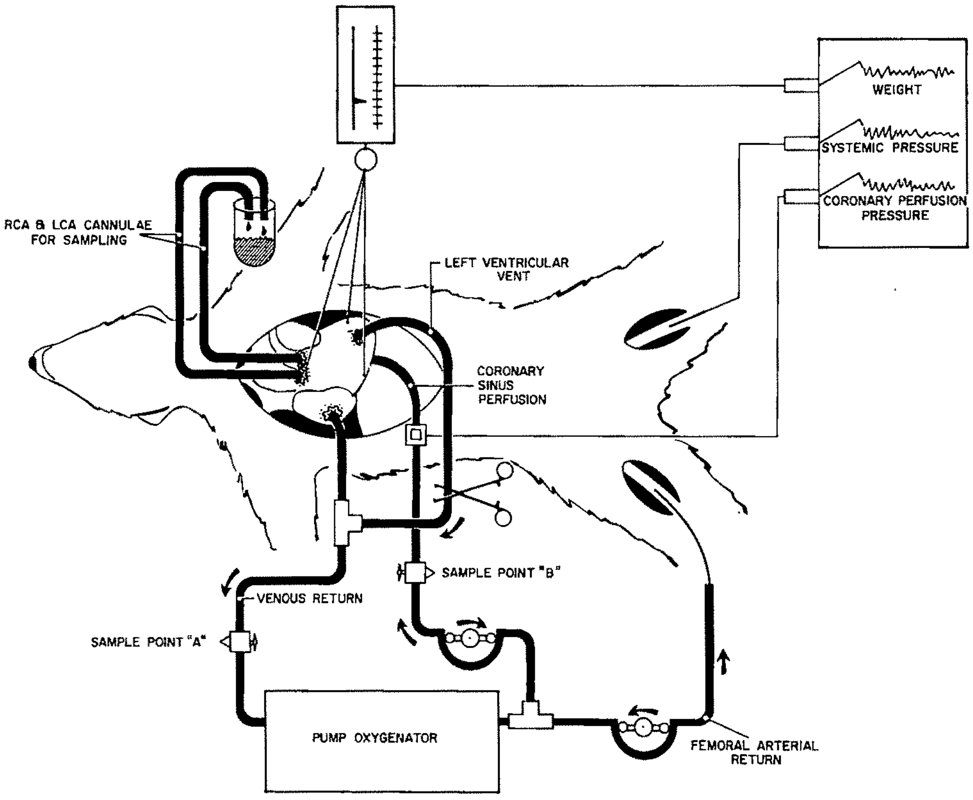


Fig 3. In vivo retrograde cardiac perfusion system used in Groups III and IV. (RCA = *right coronary artery; LCA = left coronary artery.)*

atrium, and retrograde perfusion of the heart with a separate pump through the saphenous vein segment was maintained at a flow of 50 ml per minute. The left ventricle was vented by an apical catheter as the aortic cross-clamp was removed (see Figure 3). When vigorous cardiac activity returned, the pump oxygenator was slowly discontinued, the left ventricular vent was clamped, and the heart was allowed to maintain the animal's systemic pressure with its only blood supply provided by retrograde perfusion through the coronary sinus. Heart weight, coronary sinus perfusion pressure, mean arterial pressure, and arterial and venous oxygen saturations of the coronary perfusate were determined and recorded as shown in Table 2 and Figures 4 and 5.

The hearts initially beat vigorously on retrograde perfusion, but when they were subjected to the systemic load with the ventricular vent clamped, they quickly became swollen and discolored and oxygen extraction decreased. All the hearts fibrillated shortly after the 15-minute recording time.

Group IV—In Vivo Studies with Phenoxybenzamine

Five animals were placed on cardiopulmonary bypass and arrangements for retrograde venous perfusion with left ventricular venting were carried out exactly as in Group III. However, just before retrograde perfusion was initiated, phenoxybenzamine, 1 mg/kg, was added to the coronary sinus perfusate. When vigorous cardiac activity resumed, the animals were weaned

Table 2. In Vivo Studies in Animals Subjected to Retrograde Venous Perfusion for Myocardial Revascularization

Group & Study Method	Time (min)	Pressure (mm Hg)	Weight (% increase)	AV O_2 Diff. (% saturation)	Mean Arterial Pressure (mm Hg)
Group III	0	45 ± 10	100 ± 0	33.8 ± 4.3	81.6 ± 10.2
(controls					
without phenoxy-	5	113.2 ± 34.3	112.2 ± 5.4	27.4 ± 5.2	66.8 ± 13.6
benzamine)[a]	10	132.6 ± 50.3	126.8 ± 12.2	21.8 ± 6.5	50.4 ± 10.6
	15	155.8 ± 70.4	164.4 ± 14.4	17.6 ± 7.2	32.8 ± 7.6
	20 25	Fibrillated following venting			
Group IV (animals	0	56.4 ± 8.2	100 ± 0	27.4 ± 5.6	63.0 ± 5.7
treated with	5	49 ± 2.2	102.6 ± 1.8	28.4 ± 5.9	60.0 ± 6.1
phenoxy-	10	50.6 ± 3.8	105.8 ± 5.4	25.4 ± 8.3	53.6 ± 7.4
benzamine)[a]	15	54.6 ± 5.5	107.4 ± 4.3	23.0 ± 6.4	43.0 ± 5.7
	20	55.0 ± 8.7	108.8 ± 4.4	27.0 ± 2.7	53.0 ± 2.7
	25	68.0 ± 8.4	113.8 ± 4.8	17.0 ± 4.3	37.0 ± 4.5
Groups III & IV: statistical analysis (t-test)	0	$t = 6.7$ $(p < 0.001)$	...	$t = 2.03$	$t = 3.56$
	5	$t = 4.2$ $(p < 0.01)$	$t = 3.7$ $(p < 0.01)$	$t = 0.3$	$t = 1.02$
	10	$t = 3.6$ $(p < 0.01)$	$t = 3.5$ $(p < 0.01)$	$t = 0.76$	$t = 0.55$
	15	$t = 3.2$ $(p < 0.02)$	$t = 8.3$ $(p < 0.001)$	$t = 1.25$	$t = 2.4$
	20	No comparison			
	25	No comparison			

[a] Mean of 5 animals with one standard deviation.

AV = arteriovenous.

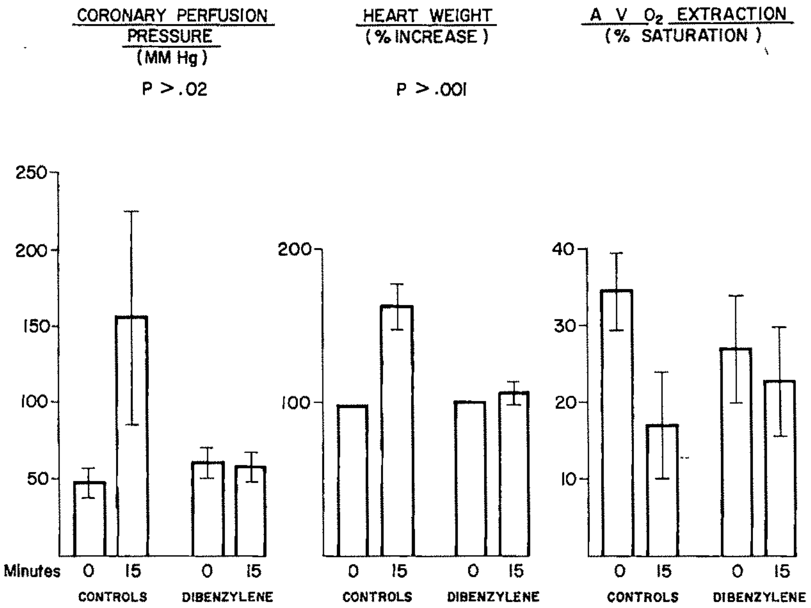
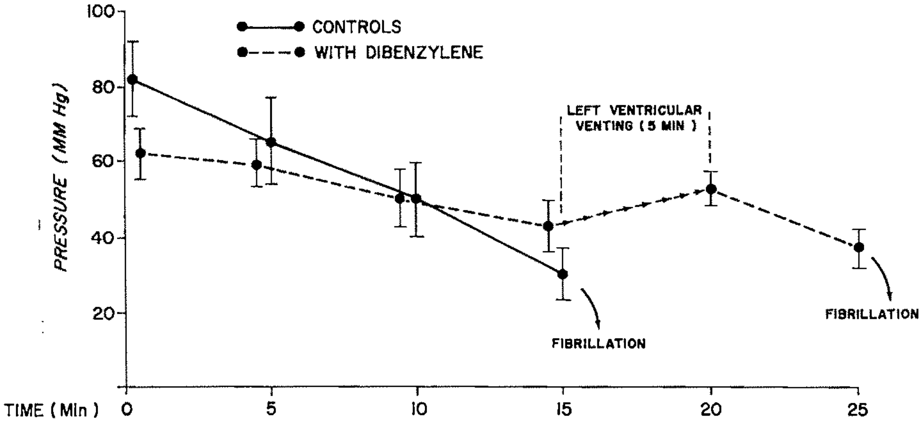


Fig 4. Comparison of in vivo control animals (Group III) with dibenzylene (phenoxybenzamine)-treated animals (Group IV).

from cardiopulmonary bypass and the ventricular vent was clamped. The hearts were then allowed to support the systemic circulation to the 15-minute recording time, at which point the hearts had not become swollen or discolored, although the systemic pressure was maintained poorly. The left ventricle was then vented and the dog was placed back on cardiopulmonary bypass for a 5-minute rest period; then the procedure of coming off bypass and allowing the heart to support the systemic load was again repeated. These data are recorded in Table 2 and appear in graph form in Figures 4 and 5.

Fig 5. Mean arterial pressure measured in in vivo control animals (Group III) and dibenzylene (phenoxybenzamine)-treated animals (Group IV).



Results

The Group I ex vivo control animals confirmed previous investigative findings [10]. In these animals, the coronary perfusion pressure, which began at an acceptable average of 38 mm Hg (previous studies having shown that pressures of greater than 50 to 60 mm Hg in the coronary venous system invariably lead to a hemorrhagic myocardium), quickly rose to an average of 136 mm Hg at the end of one hour of perfusion [9, 11]. The myocardial weight increased more than 300% (120 to 375 gm), and the arteriovenous oxygen saturation difference decreased (see Table 1, Fig 2). The hearts were grossly hemorrhagic and edematous, and while they did beat vigorously at the beginning of the retrograde venous perfusion, they were contracting quite feebly at the end of one hour. We noted that the majority of the retrograde-perfused blood (which was maintained at a constant flow of 50 ml/min) passed through the myocardium into the cardiac chambers and drained out of the various cardiac openings into the funnel collecting device. Only a small portion of the blood passed through the venoarterial communications to emerge from the coronary artery cannulas. The hearts became more visibly hemorrhagic and edematous as the perfusion progressed, and blood flow from the coronary artery cannulas diminished further. Histological sections of the myocardium revealed gross interstitial edema and hemorrhage.

The initial vascular resistance in Group I was 2,950 dynes sec/cm^{-5} and increased to 10,540 following 60 minutes of perfusion. We speculated that the increased vascular resistance had developed on the arterial side of the capillaries, and this possibility was investigated in the Group II animals, whose cardiac perfusate contained phenoxybenzamine. Several significant differences were recognized, as noted in Table 1 and Figure 1. The initial perfusion pressure for Group II was similar to that of Group I, averaging 33.4 mm Hg; however, the pressure had increased to only 42.8 mm Hg at the end of one hour, and only a minor increase in average weight (304 to 355 gm) was measured. The initial resistance was 2,561 dynes sec/cm^{-5} for Group II and increased to only 3,261 at one hour of perfusion. Oxygen extraction by the myocardium appeared to be enhanced in Group II as the arteriovenous oxygen saturation difference progressively increased. Blood flow from the coronary artery cannulas increased, and the hearts at one hour appeared strikingly different from those in Group I, ie, they were pink and beating vigorously. Pressure, weight, and arteriovenous oxygen differences were all statistically significant at 30 minutes and one hour, as noted in Table 1.

The question of performance of the myocardium perfused retrograde under systemic loading remained, and the subsequent studies in Groups III and IV were undertaken to evaluate this problem. The Group III animals served as controls, and Table 2 indicates their similarity to the Group I ex vivo controls. The coronary perfusion pressure increased from 45 to 155 mm Hg (almost 400%) during 15 minutes of retrograde perfusion. Resistance increased from 3,500 to 12,020 dynes sec/cm^{-5}. In the 15-minute period monitored for Group III (versus one hour for Group I), the weight increased only 164%. Arteriovenous oxygen extraction decreased from 33.8 to 17.6% during the 15 minutes of recording, and the mean arterial pressure fell from 81.6 to 32.8 mm Hg. In contrast to the Group I controls, hearts in the in vivo control group (with the added burden of attempting to support systemic arterial pressure) developed high perfusion pressure, increased weight, and decreased arteriovenous oxygen extraction and became edematous and discolored much more quickly (15 minutes versus 60 minutes) (see Figs 4, 5). Shortly after the 15-minute sampling time the Group III hearts developed ventricular fibrillation, which was usually preceded by rapid tachycardia or irregular beating, and they could not be defibrillated.

Group IV animals were studied exactly the same way as Group III animals except that phenoxybenzamine, 1 mg per kilogram of dog body weight, was added to the perfusate. Table 2 and Figures 4 and 5 show that the phenoxybenzamine-treated animals experienced a slight decrease in coronary perfusion pressure at the 15-minute measuring time, a minimal increase in heart weight, and much less decrease in arteriovenous oxygen extraction than the Group III animals. Resistance decreased from 4,360 to 4,190 dynes sec/cm^{-5}. While the initial mean arterial pressure in Group IV was somewhat lower than that in the Group III animals due to the phenoxybenzamine, it was later maintained at a higher level (see Fig 5). A decrease in mean arterial pressure at 15 minutes stimulated ventricular venting and support of the animal on cardiopulmonary bypass for 5 minutes while the ventricle was rested. The animals could then be weaned from cardiopulmonary bypass again with a mean arterial pressure of 53 mm Hg for the group, which decreased to 37 mm Hg 5 minutes later. This procedure of rest and subsequent pump withdrawal was repeated a number of times before it eventually resulted in irreversible fibrillation. Even at the point of irreversible fibrillation the hearts did not appear swollen or discolored, and the mean coronary sinus perfusion pressure had not increased significantly. As in the ex vivo group, the differences in pressure and weight between the control and the phenoxybenzamine-treated animals were statistically significant, as shown in Table 2.

Comment

The possibility of venous access to the myocardium has been known since Vieussens demonstrated direct communications between the coronary arteries and veins and the cardiac chambers in 1706. These became known as the thebesian veins following further description by Thebesius in 1708 [12]. The detailed descriptions of Grant and Vicko in 1929 confirmed their location to be most often on the right ventricular surface of the septum and on the left ventricular papillary muscles [8]. Later, in 1953, Gregg demonstrated that only 64 to 83% of the coronary arterial supply drains by way of the coronary sinus, confirming that some form of direct drainage to the cardiac chambers must provide for the remainder [9].

Treatment of myocardial ischemia by venous arterialization was studied experimentally by Pratt in 1898, who used the thebesian as well as the coronary veins [5]. More extensive studies were reported by Beck and co-workers in 1948 [1]; they used arterialization of the entire coronary sinus to reduce mortality in animals following ligation of three major coronary artery divisions. Arterialization of the coronary sinus in combination with its partial ligation became known as the Beck II procedure and was carried out in several patients with reportedly encouraging results, although clinical acceptance did not follow [1, 6]. Protection of selected areas of the myocardium by perfusion of a specific coronary vein with oxygenated blood was first demonstrated in dogs by Kwan-Gett in 1970 [12].

Clinical application of revascularization by use of the venous network has recently been stimulated by the problem of patients with severe angina and diffuse coronary arteriosclerosis that prevents conventional aortocoronary bypass grafting. Clinical improvement following venous revascularization in small numbers of patients has been reported by Benedict [2] and Park [13] and their associates. Benedict's 3 patients demonstrated patency in 2 of 4 grafts when studied postoperatively, and all patients were partially or completely relieved of their symptoms. Park used internal mammary artery–left anterior descending vein anastomoses in 6 patients, 4 of whom also had conventional vein grafts to the right coronary artery. All grafts to the veins were said to be open at the time of discharge, and 2 of the 6 patients were restudied at 2½ and 7 months postoperatively and were found to have patent internal mammary artery–coronary vein grafts at that time.

Clinically, the effectiveness of retrograde venous cardiac perfusion has been evaluated only by angiographic confirmation of patency, clinical improvement in the patient's angina, and myocardial scanning to demonstrate radioactivity in the region served by the grafts. Patent grafts and evidence of radioactivity can only indicate that the blood is entering the myocardium in the region of grafting, but they do not demonstrate that the oxygen supply of the myocardial cells is being enhanced. Clinical improvement of the patient suggests that the needs of the myocardial cells are being met, but this is somewhat indirect evidence, and only small numbers of patients so treated are available at this time for evaluation.

Laboratory evidence of enhanced myocardial cellular oxygen supply by retrograde venous perfusion has been reported by Bhayana and colleagues [3], who demonstrated reversal of electrocardiographic evidence of myocardial ischemia by arterialization of the anterior descending coronary vein followed by ligation of the anterior descending coronary artery. Epicardial electrocardiograms demonstrated attenuation of S-T segment elevation when the vein graft was opened and elevation of S-T segments when the graft was occluded. This is a short-lived phenomenon, however; and if retrograde venous perfusion is allowed to continue over a period of hours, the area of myocardium supplied by the vein becomes stiffened and hemorrhagic, and death of the animals results [10].

Temporary protection of the myocardium with retrograde coronary sinus perfusion during cardiovascular procedures was suggested by Blanco and associates in 1956 [4], and the technique was later endorsed clinically and experimentally by Gott and co-workers [7]. A careful evaluation of the effectiveness of myocardial protection in the dog with retrograde coronary sinus perfusion during left coronary artery occlusion was reported by Hammond and coworkers in 1967 [10]. This group demonstrated minimal impairment of left ventricular function following one hour of retrograde coronary sinus perfusion during complete occlusion of the left main coronary artery. Perfusion pressure was found to be critical, and when it exceeded 60 mm Hg a hemorrhagic and stiffened myocardium developed. Postoperative left ventricular function studies in animals protected with retrograde venous perfusion during left coronary artery occlusion showed that their hearts were only slightly impaired in comparison to animals not so protected.

The concept of low-flow, low-pressure, retrograde coronary sinus perfusion as a means of myocardial protection has recently been combined with moderate hypothermia (29°C) by Poirier and associates [14]. Their work demonstrated significantly better postoperative left ventricular performance in animals protected with the combination of retrograde coronary sinus perfusion and hypothermia.

These studies suggest that protection of the myocardium by retrograde venous perfusion can be accomplished during periods of interrupted coronary artery blood flow and that the myocardium thus protected can resume effective work when coronary arterial blood flow is reestablished. It would still appear to be unresolved whether retrograde venous myocardial perfusion is adequate as the sole supply of blood while the ventricle is maintaining the systemic load. This question served as the basis of the present study.

Conclusions

Cardiac activity can be maintained both ex vivo and in vivo with retrograde venous perfusion. Ex vivo untreated hearts become swollen, edematous, and discolored, and they beat poorly at the end of one hour of retrograde perfusion. These changes occur much more quickly in the in vivo heart supporting the systemic circulation. Treatment of both ex vivo and in vivo retrograde-perfused hearts with phenoxybenzamine extends the period of vigorous activity and attenuates the marked increase in perfusion pressure and weight seen in untreated hearts. However, the treated in vivo retrograde-perfused hearts could not maintain the systemic circulation of dogs for longer than 25 minutes, even with intermittent rest provided by left ventricular venting during cardiopulmonary bypass support. The data suggest that extensive myocardial revascularization by the retrograde venous route would be ineffective in patients.

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Use of Profound Hypothermia Induced by Surface Cooling in Open-Heart Surgery

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ABSTRACT **Profound hypothermia with body-surface cooling for use in open-heart surgery is considered a difficult anesthetic technique because of the problems of controlling ether anesthesia. This paper describes our hypothermia technique in detail, with emphasis on its particular usefulness in open-heart procedures in neonates and infants. The results are based on our experience with 281 consecutive patients. Guidelines for safe and effective performance of this technique were established on the basis of continuous monitoring of the electrocardiogram, electroencephalogram, and arterial blood pressure. We conclude from our experience that open-heart operation under profound hypothermia is a safe, effective, and extremely promising method.**

Over the past ten years the results of open-heart operations for various cardiac conditions have shown marked improvement, largely due to the development of extracorporeal circulation as an auxiliary method during operation. Extracorporeal perfusion during open-heart procedures does have some disadvantages, in that a considerable amount of supplementary blood is required and a completely bloodless and motionless operative field is difficult to obtain. Therefore, since 1968 we have performed most open-heart operations under hypothermia induced by body-surface cooling. The advantages of this method are: (1) minimal hemorrhage during the operative procedure; (2) a completely bloodless and motionless operative field; and (3) ease of postoperative respiratory care as well as a low incidence of pulmonary complications. In Japan, a study of this method was initiated by Watanabe in 1952 [9], and rapid development of the technique in line with his suggestions culminated in the first successful clinical applications in 1958 [3].

The purpose of this paper is to describe the technique we use for inducing profound hypothermia and to analyze in depth our results with 281 patients.

Materials and Methods

Our 281 patients underwent open-heart operations under profound hypothermia induced by body-surface cooling in Yokohama City University Hospital from January, 1968, through December, 1974 (Table). Ages ranged from 1 month to 28 years with a mean of 4.6 years. Infants and children are good candidates for this method, and pediatric patients predominate in our series.

Anesthesia

The method of anesthesia has been reported elsewhere [5]. As a rule, however, we follow the method advocated by Okamura [3, 7], which will be described in detail.

Intramuscular injections of triflupromazine, 0.15 mg per kilogram of body weight, and Pethilorfan (pethidine and levallorphan), 0.5 to 1.0 mg/kg, are given 1½ hours prior to initiation of anesthesia. One hour prior to induction, hydroxyzine, 0.5 to 1.0 mg/kg, and atropine, 0.005 to 0.007 mg/kg, are administered intramuscularly. Triflupromazine, Pethilorfan, and hydroxyzine are repeated in the same dosages 30 minutes prior to the onset of anesthesia.

In infants and small children, ketamine hydrochloride, 4 mg/kg, is given intramuscularly for induction of anesthesia, while in adults 300 to 400 mg of thiopental sodium is administered intravenously. Finally, 20 to 30 minutes prior to anesthesia induction and the start of body cooling, another dose of triflupromazine, 0.5 mg/kg, is given intravenously.

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Patients Undergoing Open-Heart Operations Using Profound Hypothermia with Surface Cooling

Anomaly	No. of Patients 1968	1969	1970	1971	1972	1973	1974	Total Patients	Mortality (%)
VSD	7	8	7	22	11	6 (1)	3	64 (1)	1.6
VSD with PH	5 (2)	2	9 (1)	8	10	5	6	45 (3)	6.7
VSD with PS	1		2	1	3	2 (1)	4	13 (1)	7.7
VSD & ASD				1			1	2	0
VSD, ASD, & PS						1		1	0
VSD & PDA			1					1	0
VSD & PDA with PH			1		1	1	2	5	0
ASD	4	1	4	9	13	10	11	52	0
PS	1	1		1	1	1	3	8	0
PS with ASD	4 (1)	2	1	2	3	2		14 (1)	7.1
ECCD	1 (1)			1 (1)		1		3 (2)	66.7
TAPVR			1 (1)	1 (1)			2 (1)	4 (3)	75
T/F	13 (7)	2 (1)	8 (2)	10 (5)	6 (1)	6	8 (1)	53 (17)	32
BVRV (double-outlet)	1 (1)				1 (1)	1		3 (2)	66.7
PA			1 (1)					1 (1)	100
Truncus arteriosus			1 (1)					1 (1)	100
Coarctation complex			2 (1)			2 (2)		4 (3)	75
AI				1				1	0
VSD with AI							1	1	0
MI							2	2	0
Miscellaneous				2 (2)	1			3 (2)	66.7
Total	37 (12)	16 (1)	38 (7)	59 (9)	50 (2)	38 (4)	43 (2)	281 (37)	13.2

Numbers in parentheses represent deaths.

VSD = ventricular septal defect; PH = pulmonary hypertension; PS = pulmonary stenosis; ASD = atrial septal defect; PDA = patent ductus arteriosus; ECCD = endocardial cushion defect; TAPVR = total anomalous pulmonary venous return; T/F = tetralogy of Fallot; BVRV = origin of both great vessels from the right ventricle; PA = pulmonary atresia; AI = aortic insufficiency; MI = mitral insufficiency.

In order to prevent possible blood sludging during hypothermia, 15 ml/kg of low-molecular-weight dextran is instilled by intravenous drip during the process of cooling. At the time of occlusion of the major vessels, Young's solution,* 0.8 to 1.0 ml/kg but not to exceed 20 ml at one time, is injected into the aortic root to induce cardiac standstill. The aortic clamp is released and the cardiac resuscitation solution,† 1.0 ml/kg but not to exceed 20 ml at one time, is injected into the left ventricle through the apex. Heparin, 1.5 mg/kg, is administered when the esophageal temperature falls below 30°C. Protamine sulfate, 1.5 mg/kg, is usually given when the body temperature has returned to approximately 27°C and sinus rhythm has been restored.

Following endotracheal intubation, rapid ether inhalation is started within a closed circuit. The patient is thus quickly brought into Stage III, Plane I, status (the lightest stage of surgical anesthesia) within 3 to 5 minutes of ether inhalation. Ether inhalation can be continued by way of the patient's spontaneous respiration. The patient should reach Stage III, Plane III, status (deep anesthesia) and remain there throughout the course of hypothermia.

Though the relationship between the ether inhalation dosage and the decline in body temperature cannot be strictly defined, 2.0 cc/kg of ether inhaled at 30°C, 2.5 cc/kg at 25°C, and 3.0 cc/kg upon reaching the target body temperature are recommended, with further adjustment thereafter. Due to the inevitable leakage of ether from the anesthesia machine, 3.5 to 4.0 cc/kg is sometimes required at the final stage. We calculate the precise dosage of ether to be inhaled on the basis of changes in arterial blood pressure, the electrocardiogram, and the electroencephalogram.

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*Young's solution: 0.81 gm of sodium citrate and 2.46 gm of magnesium sulfate dissolved in 100 ml of water with pH adjusted to 7.4.

†Cardiac resuscitation solution: 10 ml of 20% glucose in water, 100 ml of 2% $CaCl_2$, and 1.0 ml of 0.1% norepinephrine.

During anesthesia, the following are monitored either continuously or intermittently: electroencephalogram (bipolar frontal leads); electrocardiogram (mostly lead II); arterial blood pressure (femoral or brachial artery); central venous pressure; oxygen tension (Po_2); carbon dioxide tension (Pco_2); pH; and hematocrit for both arterial and venous blood. Blood gas analysis is carried out using the Astrup radiometer.*

Hypothermia Technique

It should be noted that the mode of anesthesia described is designed specifically for profound hypothermia in connection with an open-heart operation. Cooling is usually started when the anesthesia status reaches Stage III, Plane II (moderate surgical anesthesia); the time required to reach this state is about 10 minutes. The conventional dose of ether inhaled initially from intubation to the beginning of cooling is 1.0 cc/kg. Subsequent doses should be titrated according to the method previously described. The usual maintenance dose of ether is in the range of 3.0 to 3.5 cc/kg.

During cooling, the speed of ether inhalation must be carefully adjusted in order to avoid extremely slow cardiac rhythm or standstill. As the target body temperature of 20°C is approached, the patient is removed from the ice-water bath at 23°C to avoid further cooling. Occasionally we have worked with a patient at a body temperature of slightly over 20°C. The heart rate and rhythm in these patients remain favorable, and no adverse change is noted even when the heart is palpated directly or an intracardiac maneuver is carried out. We believe this is due to the unique antiarrhythmic properties of ether.

As shown in Figure 1, arterial pressure and pulse rate decrease steadily along with the fall in body temperature. It should be noted that despite the decline in arterial pressure, adequate pulse pressure is maintained. In the presence of satisfactory peripheral circulation as well as sufficient pulse pressure, complications such as postoperative cerebral damage due to circulatory insufficiency are avoided. Following occlusion of the superior and inferior venae cavae, sufficient manual pressure is applied to the lung so that blood in the heart and lungs can be diverted to the systemic circulation. The aorta is then clamped. This is followed by an injection of 0.8 ml/kg of Young's solution into the root of the aorta. As soon as cardiac standstill is achieved, the intracardiac procedure can be started. At cardiotomy, the small amount of blood remaining in the cardiac chambers is suctioned out; it should be retransfused to the patient following resuscitation, thus minimizing the amount of new blood needed.

When the operation nears completion, warm water (about 45°C) is poured into the bathtub for reversion of the body temperature. At the end of the procedure the platform is kept lowered, and the patient is warmed while floating in warm water. Air in the cardiac cavity must be completely removed before the aortic clamp is released. After several applications of cardiac massage, 1 ml/kg of the cardiac resuscitating agent is introduced through the apex into the left ventricle. At this point the assistant compresses the ascending aorta to ensure effective inflow of the agent through the coronary arteries. Aortic occlusion, including cardiac anoxia, may be continued safely for up to 60 minutes at 20°C or 30 minutes at 25°C according to our experience.

During rewarming, the blood drawn from the cardiac cavities during hypothermia is transfused back to the patient. At the actual operation little hemorrhage occurs, and therefore retransfusion of the patient's own blood frequently suffices for blood replacement. Rewarming usually proceeds in a manner analogous to the process of cooling. Regular sinus rhythm is reestablished at around 30°C. The rewarming process is terminated upon reaching the target temperature of 35° to 36°C. Since optimal rewarming can

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*Astrup Manufacturing Co, Copenhagen, Denmark.

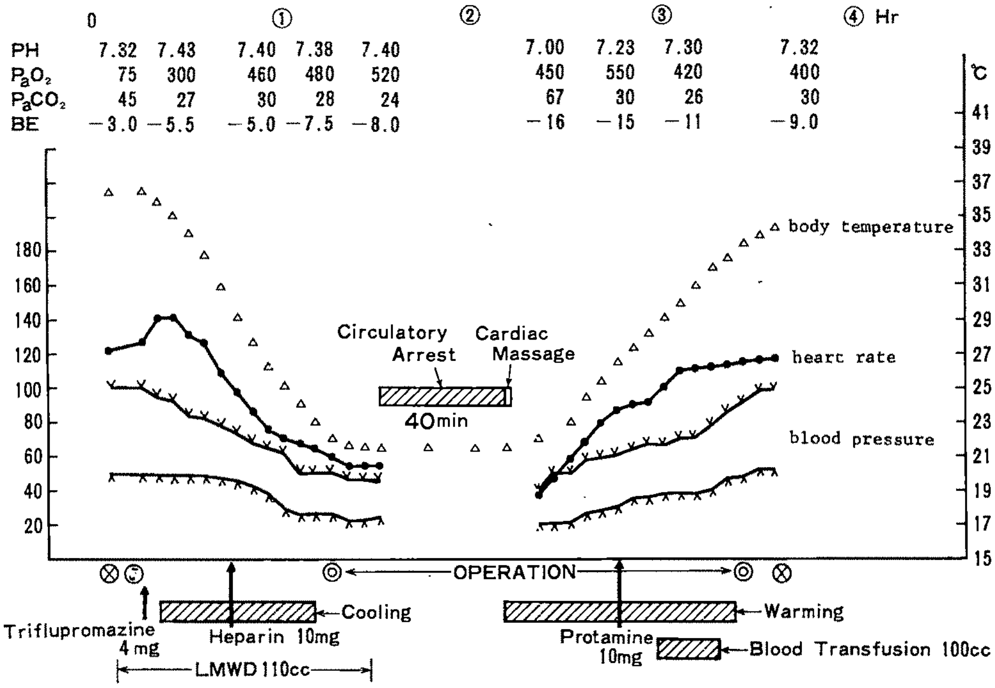

Fig 1. Typical course of an open-heart operation under profound hypothermia. Alterations in physiological variables prior to, during, and immediately after the procedure are shown. The patient is an 11-month-old boy weighing 5,700 gm who had a ventricular septal defect and severe pulmonary hypertension. (BE = *base excess;* LMWD = *low-molecular-weight dextran.)*

usually be achieved near the end of the operation, anesthesia need not be unduly prolonged.

An additional advantage of this type of hypothermia lies in the relative ease of postoperative respiratory control. Spontaneous respiration resumes almost immediately after the operation, and we have seldom encountered a patient who required postoperative ventilation.

Results

There were 37 operative deaths (13.1%) among the 281 patients undergoing open-heart operations using profound hypothermia. Among the patients operated upon in 1968 there were some whose cardiac resuscitation proved difficult. In 3 patients cerebral damage ensued, probably due to lack of refinement in the hypothermia technique [5]. With subsequent improvement in the method, however, these complications subsided, and we have encountered none since 1970.

As a rule, we induced intensive hemodilution with low-molecular-weight dextran in order to prevent the sharp rise in blood viscosity associated with sludging of peripheral blood which accompanies the fall in body temperature. Accordingly, hematocrit values usually stayed between 30 and 35% throughout the course. This was true even in patients with marked cyanosis.

Blood gases and acid-base balance were measured at 38°C, and Pa_{O_2} showed considerable variation during the course of anesthesia. It is difficult to draw any conclusions from our blood gas data since these variables are prone to subtle changes, depending on the basic disease and the degree of anesthesia. Generally speaking, however, the average Pa_{O_2} during operation was found to be in the neighborhood of 400 mm Hg in patients with a left-to-right shunt. As cooling progresses, it is natural for oxygen consumption to decrease, resulting in a rise in Pa_{O_2}; a reverse trend should be seen during the rewarming process. In actuality, however, Pa_{O_2} remained continually higher than preoperative values because correction of the cardiac anomaly had already been completed at about the time rewarming was achieved.

Figures 2 and 3 show the changes in Pa_{CO_2} and pH with alterations in body temperature. The Pa_{CO_2} stayed around 40 mm Hg with a transient rise of slight degree at around 30°C, which was followed by a gradual decrease thereafter. A close relationship was evident between Pa_{O_2},

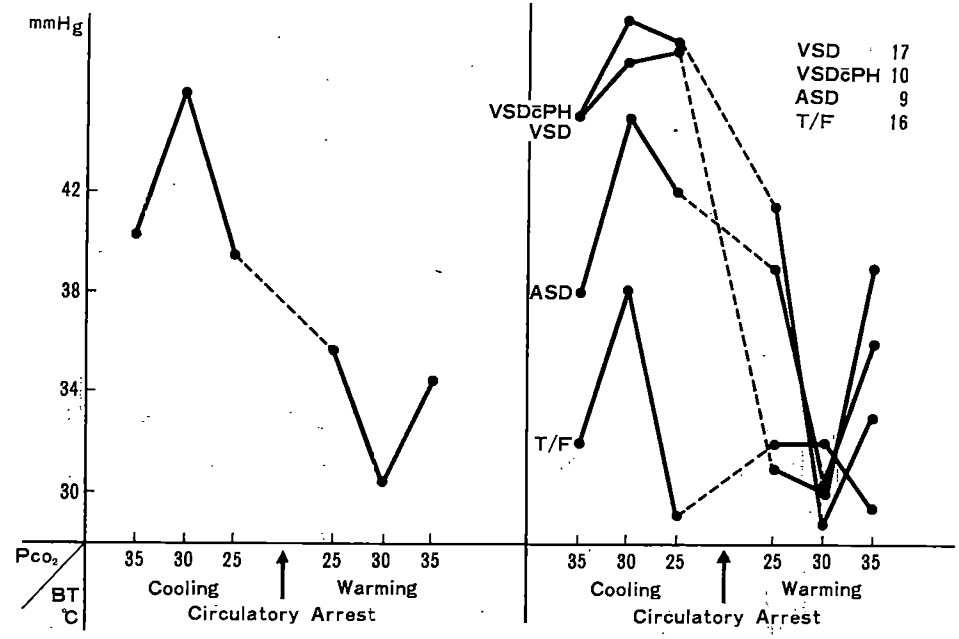

Fig 2. Changes in Pa_{CO_2} during anesthesia. (A) Average Pa_{CO_2} values in 52 patients. (B) Pa_{CO_2} in various cardiac conditions. (VSD = *ventricular septal defect;* PH = *pulmonary hypertension;* ASD = *atrial septal defect;* T/F = *tetralogy of Fallot.)*

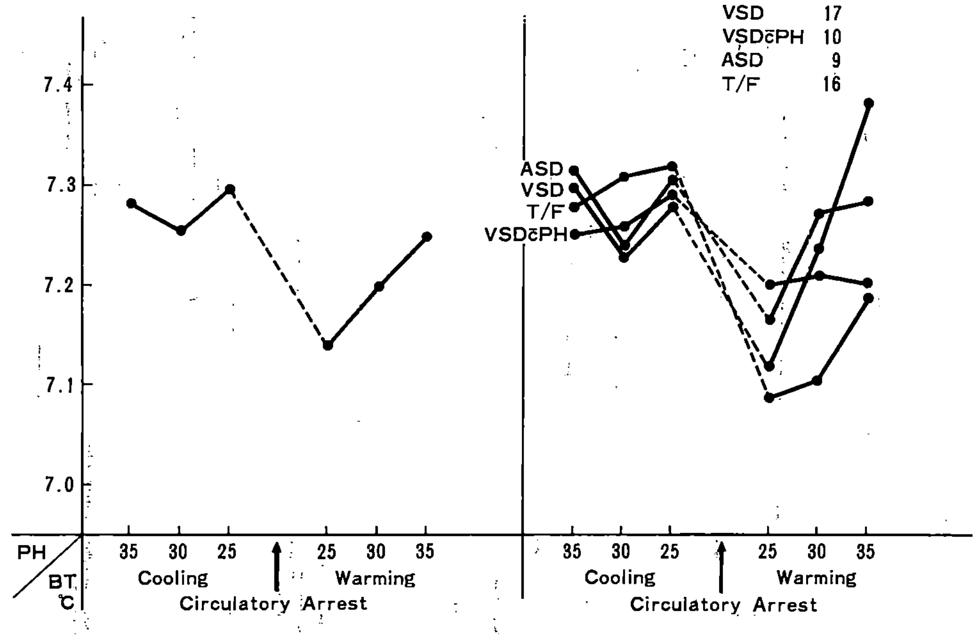

Fig 3. Changes in pH during anesthesia (measured at 38°C). (A) Average values in 52 patients. (B) Values in various cardiac conditions. (Abbreviations same as in Figure 2.)

Pa_{CO_2}, and the degree of anesthesia. Low values were sometimes obtained when hyperventilation was observed during the course of anesthesia.

As to pH and base excess, the former remained at around 7.30 during the cooling process up to the time of aortic occlusion, while the latter showed a slight decrease (Fig 4). It is not yet known whether these changes are directly related to the effect of hypothermia or to the pharmacological action of ether.

When rewarming was begun following the release of aortic occlusion, the Pa_{CO_2} showed a transient rise and pH fell suddenly, indicating the development of acidosis. It was observed that due to hyperventilation, Pa_{CO_2} values occasionally declined to a slightly lower level than in the cooling process but returned to nearly normal limits within several hours after completion of the operation. It is to be emphasized that keeping the Pa_{CO_2} as low as possible (20 to 30 mm Hg) by means of hyperventilation is mandatory in order to hold pH within the physiological range. During anesthesia, and especially in the process of rewarming, the heartbeat recovered favorably as the pH returned closer to normal values. Cardiac resuscitation was usually easy, and no major arrhythmia was encountered.

Base excess was usually negative not only during rewarming but also thereafter, which may indicate that metabolic acidosis was present. Nevertheless, no special correction was required in most of the patients. Return to normal values was generally noted several hours after operation, with the patient who had the longest delay requiring a day for recovery (see Fig 4).

Some variations were noted in serum electrolytes. The average preoperative value for sodium was 136 mEq/L; potassium, 4.3 mEq/L; and chlorine, 106 mEq/L. During the cooling process serum potassium decreased slightly in most patients, though occasionally it fell as low as 2.6 mEq/L just prior to the institution of cardiac anoxia. This trend, however, would reverse itself, and a gradual rise would begin during the process of rewarming so that at the completion of rewarming preoperative values were usually restored. Sodium and chlorine showed little change, even immediately before the cardiac standstill.

After cooling was begun, electroencephalographic waves (from bipolar frontal leads) became gradually slower in proportion to the fall in body temperature, with a characteristic decrease of rapid waves as well as a decline in amplitude. Immediately before aortic occlusion and cardioplegia, the EEG was frequently observed to be flattened, and occasionally it completely disappeared. Excessively fast inhalation of ether caused rapid suppression of the EEG; the same trend was occasionally seen with a relatively

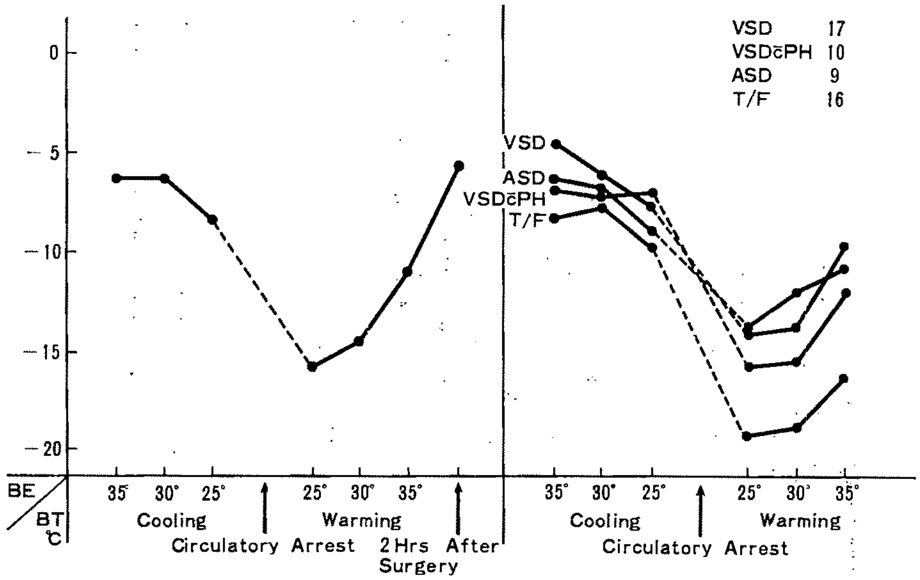

Fig 4. Changes in base excess during anesthesia (measured at 38°C). (A) Average value in 52 patients. (B) Values in various cardiac conditions. (Abbreviations same as in Figure 2.)

high body temperature. In this regard the EEG can serve as an index of the depth of anesthesia, the degree of cerebral hypoxia, and the state of the autonomic nervous system.

As body temperature fell, prolonged P-Q and R-R intervals in the electrocardiogram indicated the onset of bradycardia. As long as anesthesia was adequate, sinus rhythm was usually maintained and would be until the time of circulatory occlusion. Supraventricular arrhythmia or atrial fibrillation might occasionally supervene, but in our experience these were always due to inadequate anesthesia, and sinus rhythm was usually restored with rapid inhalation of a small amount of ether. No remarkable changes were noted in the S-T segment and T wave.

If bradycardia persists or restoration of sinus rhythm is delayed once resuscitation has begun, atrioventricular block should be considered. Right bundle-branch block can also appear after the incision has been made in the right ventricle. These abnormalities should be detected as early as possible and treated appropriately to ensure an uneventful postoperative course.

Comment

Ether anesthesia is widely used in profound hypothermia despite its explosive properties and such disadvantages as its tendency to raise secretions in the airway. This is mainly because of the fact that it possesses a unique antiarrhythmic effect. Ether can also inhibit cardiac function, however, and it is essential to keep the dose within a narrow therapeutic range in which only the antiarrhythmic effect is expressed and no suppression of cardiac function is exhibited. Since the body temperature of human beings, who are homeothermic animals, cannot be lowered below 20°C without the use of anesthesia, an investigation of the potential influence of anesthesia upon the pathophysiology of hypothermia is badly needed. At present, however, neither the basic physiology nor the biochemistry of hypothermia is clearly understood, and this is why anesthesia under hypothermia is accepted with much hesitancy.

In order to maintain desirable circulatory hemodynamics during hypothermic anesthesia, it appears that skillful induction of the anesthesia is most important. A gradual decline in arterial blood pressure and a smooth decrease of pulse rate parallel to a gradual fall in the body temperature can thus be ensured. If the anesthetic is given in insufficient quantities during the cooling process, peripheral vascular contraction is apt to occur, resulting in extensive shivering and thus imposing excessive stress on the patient that might preclude continuation of anesthesia. In order to prevent untoward occurrences during the cooling process, adequate titration of ether as well as the use of autonomic blocking agents with peripheral vasodilating action is of paramount importance. Excessively deep ether anesthesia, however, can cause peripheral circulatory insufficiency, suppression of cardiac function as manifested by an abnormal ECG, or profound hypotension. This makes subsequent cooling and resuscitation extremely difficult. It may also cause irreversible cerebral damage, and therefore one must be extremely cautious not to give an excessive amount of ether.

Ether also has the property of concentrating blood. Hypothermia further exacerbates this effect, and complications such as sludging of the blood may occur. This, however, can be effectively prevented by administration of low-molecular-weight dextran and heparin. Oxygen consumption decreases markedly during hypothermia, and cerebral damage, when it does occur, is believed to be due to the ether's effect on both blood concentration and coagulability rather than to tissue hypoxia secondary to hypothermia and the operative procedure [1].

While many studies are available on the status of acid-base balance during hypothermia, the results are not uniform. In our series base excess was often negative at the onset of anesthesia, which might have been partially due to the pharmacological action of ether, and it tended to decrease further with cooling, reaching as low as −10 mEq/L. Immediately after release of aortic occlusion, however, a reversal of this condition occurred and profound acidosis developed. It is apparent that this was due to the outpouring and subsequent circulation of acid substances that had accumulated in the tissues because of anaerobic metabolism during circulatory occlusion. This acidosis was transient, and the metabolism stabilized quickly during rewarming.

Nearly normal pH values were usually obtained relatively early in the postoperative period. Isayama [2] has pointed out that acidosis in hypothermia is not as important as it had been assumed to be and concluded that it may be connected with the nature of hypothermia per se. On the other hand, as pointed out by Mohri and co-workers [6], a more favorable anesthetic course is obtained if acidosis can be prevented before and after aortic occlusion. This is usually achieved by keeping Pa_{CO_2} low with induced hyperventilation and also by maintaining pH values at a rather high level, around 7.80, throughout the course. In any case, acid-base balance under hypothermia needs to be investigated further in light of the complex metabolic changes that take place.

Many reports are available concerning electrolyte metabolism during hypothermia. In each, electrolyte concentration does not vary widely, and its relationship with hypothermia is not clearly established as yet [8]. In our series sodium and chlorine showed few changes, and potassium was either at the lower limit of normal or slightly below it. The lowest value was encountered either at a body temperature of 24° to 25°C or at the time of circulatory occlusion. It is generally believed that changes in serum potassium level are directly related to the degree of fall in body temperature. However, the significance of this observation is as yet poorly understood.

The electroencephalogram has long been used to evaluate the depth of anesthesia. Among anesthetic agents, ether has been studied most extensively for its effect on the EEG. As the anesthesia is deepened with ether, EEG amplitude is usually increased, with a concomitant decrease in the cycle. Such a relationship is quite closely correlated, and EEG changes precisely reflect the concentration of ether in the arterial blood. In hypothermia with deep ether anesthesia the EEG does not disappear until the point immediately before aortic occlusion. Once ischemia is instituted, however, the EEG disappears within several seconds and reappears only when the body temperature rises above 30°C. There is a rapid recovery to normal after the temperature has reached 35°C.

The electrocardiogram reflects cardiac status and depth of anesthesia. When anesthesia is too deep, myocardial suppression occurs, leading to hypotension; ECG abnormalities are usually noted under such circumstances. The anesthesia should therefore be controlled within a very narrow range, and cooling should be started at the proper time; the ECG is an informative guide in determining this range. A favorable cardiac condition during the cooling process is characterized by a sustained, regular sinus rhythm with minimal S-T and T-wave changes.

According to Okamura [7], ventricular fibrillation, along with other kinds of dysrhythmias, sometimes appears during hypothermia. In most cases this is due to an increase in myocardial irritability. In our experience, however, arrhythmias in hypothermia are usually manifested in the form of supraventricular rhythm disturbances, particularly atrial fibrillation or conduction abnormalities such as atrioventricular block. We have seen no instances of ventricular fibrillation.

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Combined Valvular and Coronary Artery Surgery

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ABSTRACT **Between July 1, 1971, and March 1, 1975, 45 patients underwent combined valvular and coronary artery operation. Aortic valve disease was present in 30 patients, mitral valve disease in 13, aortic and mitral valve disease in 1, and tricuspid valve disease in 1. The average age was 57 years. Seventeen patients were in New York Heart Association Functional Class IV. Seventeen patients had had a previous myocardial infarction. Significant coronary artery disease was an unexpected finding at the time of coronary angiography in 14 patients. The average number of grafts inserted was 2.5 per patient. The grafts were placed prior to valve replacement, and periods of myocardial ischemia were kept at a minimum by maintaining coronary perfusion throughout the operation. Operative mortality was 16%; late mortality was 8%. Perioperative myocardial infarction occurred in 2 patients.**

In spite of the marked improvement in operative results following valve operations, myocardial infarction and ischemia continue to be a common cause of early and late mortality and morbidity [11, 14, 18]. The use of coronary angiography at the time of cardiac catheterization for evaluation of valvular heart disease can identify those patients with coexisting coronary artery disease. Direct revascularization by aortocoronary bypass grafting at the time of a valve procedure should decrease the operative risk and may improve the long-time result by reducing the likelihood of subsequent myocardial infarction and symptoms of ischemia. The experience with 45 patients undergoing combined valve operation and aortocoronary bypass grafting demonstrates that the combined procedure can be performed with satisfactory results.

Materials and Methods

Between July 1, 1971, and March 1, 1975, 219 patients underwent valve replacement or valvuloplasty. All patients over the age of 40 years and any younger patient with symptoms suggesting coronary artery disease were evaluated by coronary angiography at the time of cardiac catheterization. Forty-five patients were found to have significant atherosclerotic coronary artery occlusive disease and underwent aortocoronary bypass grafting with saphenous veins at the time of the valve procedure. The distribution and severity of coronary stenosis is illustrated in Table 1. Thirty patients had aortic valve replacement, 13 patients underwent mitral valve replacement or mitral valvuloplasty, 1 patient had aortic and mitral valve replacement, and 1 had tricuspid valve replacement.

Thirty-five patients were men, and 10 were women. Ages ranged between 34 and 75; the average age was 57 years. Four patients were 70 or older. The patients were classified preoperatively according to the New York Heart Association functional criteria. Seventeen patients were in Functional Class IV, 18 were in Class III, and 10 were in Class II. Twenty-eight of the patients had angina pectoris. Seventeen had had a previous myocardial infarction (Table 2).

The hemodynamic abnormalities are listed in Table 3. Fifteen patients had predominant aortic stenosis. Peak systolic gradients ranged between 40 and 100 mm Hg. Aortic regurgitation was present in 7 patients, while 8 had mixed aortic stenosis and regurgitation. Six patients had rheumatic mitral valve disease. Severe mitral stenosis was present in 5 patients and mitral regurgitation in 1. Two patients had ruptured chordae tendineae; this resulted from myxomatous degeneration of the mitral valve apparatus in 1 patient and ischemic heart disease in the other. Five patients had papillary muscle dysfunction and 1 had papillary muscle

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Table 1. Distribution and Severity of Coronary Artery Disease in 45 Patients Undergoing Combined Valvular and Coronary Artery Operation

Valve Replaced & Severity of Coronary Artery Occlusion	Coronary Artery			
	L Main	LAD	Circ.	RCA
Aortic				
Total occlusion	...	1	1	4
75–99%	1	15	13	5
50–74%	2	10	4	7
Mitral				
Total occlusion	...	1	3	5
75–99%	...	6	3	4
50–74%	...	3	5	4
Aortic & mitral				
75–99%	...	1	...	1
Tricuspid				
75–99%	...		1	1

LAD = left anterior descending coronary artery; circ. = circumflex coronary artery; RCA = right coronary artery.

rupture, all secondary to ischemic heart disease. The patient with tricuspid valve disease had Ebstein's anomaly with an atrial septal defect and a right-to-left shunt.

The operative technique remained standardized. Each portion of the operative procedure was done separately and in sequence. The aortocoronary bypass grafts were always performed prior to the valve replacement. The proximal aortic-saphenous vein anastomosis was done as the initial part of the procedure. Cardiopulmonary bypass was then instituted using hemodilution, mild hypothermia (32° to 34° C), and a disposable bubble oxygenator. Ventricular fibrillation was induced, and the left ventricle was decompressed through the right superior pulmonary vein. The saphenous vein–coronary artery anastomosis was then performed. While the anastomosis was being done, the coronary artery was occluded temporarily by compression to control bleeding from the arteriotomy. The aorta was cross-clamped only when aortic regurgitation was present. In this situation, the aorta was opened and the coronary arteries were perfused with cannulas inserted in the coronary ostia. Following completion of all of the coronary bypass grafts, valve replacement or valvuloplasty was performed.

An average of 2.5 grafts per patient was performed. The number of grafts ranged from a single graft in 10 patients to 5 grafts in 2 patients. The aortic valve was replaced in all patients with either a Starr-Edwards (Model 1260 and Model 2320) or a Björk-Shiley prosthesis. Mitral valve replacement was performed in 8 patients with a Starr-Edwards prosthesis (Model 6320) and in 2 patients with a porcine xenograft. Three mitral valvuloplasties were performed. The tricuspid valve was replaced with a porcine xenograft.

Results

Operative and late mortality is presented in Table 4. Five early deaths occurred following aortic valve replacement. Two deaths were due to left ventricular failure and occurred in patients with previous myocardial infarction who were in severe congestive heart failure prior to operation. The 3 remaining deaths were due to uncontrolled bleeding at operation, hemorrhagic pancreatitis occurring 10 days postopera-

Table 2. Presence of Angina or Previous Myocardial Infarction in 45 Patients Undergoing Combined Valvular and Coronary Artery Operation

Valve Replaced	No. of Patients	Angina	Previous MI
Aortic	30	21	10
Mitral	13	6	6
Aortic & mitral	1	0	0
Tricuspid	1	1	1
Total	45	28 (62%)	17 (38%)

MI = myocardial infarction.

Table 3. Hemodynamic Abnormalities in 45 Patients with Combined Valvular and Coronary Artery Disease

Valve & Type of Disease	No. of Patients
Aortic	
Stenosis	15
Regurgitation	7
Mixed	8
Mitral	
RHD, stenosis	5
RHD, regurgitation	1
Ruptured chordae	2
Papillary muscle dysfunction	5
Papillary muscle rupture	1
Tricuspid	
Ebstein's anomaly	1

RHD = rheumatic heart disease.

tively, and fungal endocarditis occurring 30 days postoperatively, respectively. There were 2 early deaths following mitral valve replacement. Both occurred in patients in congestive heart failure with papillary muscle dysfunction following myocardial infarction.

There were 3 late deaths. Three months following aortic valve replacement, a patient developed thrombocytopenia while receiving quinidine and died following an intracerebral hemorrhage. A second patient with a long history of rheumatic heart disease and congestive failure died 1 year after mitral valve replacement with progression of heart failure. There was no evidence of dysfunction of the prosthetic valve or of failure of the vein grafts at postmortem examination. The third patient died with left heart failure and multiple arrhythmias 15 months following mitral valve replacement for papillary muscle dysfunction. Left ventricular function was markedly impaired prior to operation and failed to improve postoperatively.

Myocardial infarction as demonstrated by the appearance of new Q waves on the electrocardiogram postoperatively occurred in only 2 patients. Both patients had had aortic valve replacement and had an uncomplicated recovery following operation despite evidence of a perioperative myocardial infarction. Evidence of myocardial necrosis demonstrated by cardiac enzyme elevation was not obtained on a routine basis in any of the patients.

Comment

The routine use of coronary angiography in the evaluation of patients with valvular heart disease has demonstrated that a significant number of patients have coexisting coronary artery occlusive disease. The reported incidence of coronary occlusive disease in patients with valvular heart disease varies between 7 and 48% [7, 13]. A number of reports indicate that patients with combined valvular and coronary artery disease always have angina [3, 6]; they conclude that the increased workload imposed by the valvular lesion produces an increased myocardial oxygen demand and precipitates symptoms of myocardial ischemia. A definite history of angina, however, was present in only 28 (62%) of our

Table 4. Mortality and Incidence of Postoperative Infarction in 45 Patients Undergoing Combined Valvular and Coronary Artery Operation

Type of Operation	No. of Patients	Postoperative Deaths		Late Deaths	
		No.	%	No.	%
AVR, ACBPG	30	5	17	1	3
MVR, ACBPG	13	2	15	2	8
AVR, MVR, ACBPG	1	0	0	0	0
TVR, ACBPG	1	0	0	0	0
Total	45	7	16	3	8

AVR = aortic valve replacement; MVR = mitral valve replacement; TVR = tricuspid valve replacement; ACBPG = aortocoronary bypass graft.

patients (see Table 2). In 14 patients (31%), significant coronary artery disease was an unexpected finding at the time of coronary angiography. This finding supports the policy of performing coronary angiography routinely during the evaluation of valvular heart disease in spite of the absence of angina.

Various reports have demonstrated that valve replacement can be combined successfully with coronary bypass grafting [2, 5, 15–17]. While some reports have indicated that the operative risk is considerably higher than the risk with either isolated valve replacement or coronary bypass grafting, other reports have demonstrated that the operative risk for the combined operation is essentially the same as that for either operation alone [4, 8]. In our series the operative mortality for the combined operation (16%) exceeds the current risk of isolated valve replacement or bypass grafting alone [1, 10, 12]. Whether the combined operation has a significant effect in decreasing operative and late mortality cannot be determined without having the opportunity to compare these patients to a group of patients with comparable coronary artery disease undergoing valve replacement alone. Only 2 of the operative deaths in the patients undergoing aortic valve replacement were due to myocardial factors. Both of these patients had had previous myocardial infarctions and had diffuse three-vessel coronary artery disease demonstrated angiographically. One of the patients had severe aortic stenosis with an 80 mm Hg gradient and evidence at postmortem examination of a recent myocardial infarction. The other patient had severe aortic regurgitation, three-vessel coronary disease, and an aneurysm of the aortic arch. Both were in Functional Class IV. The remaining 3 deaths following aortic valve replacement were due to either technical or noncardiac factors. The 2 deaths occurring after mitral valve replacement were due to myocardial failure. Both patients had had previous myocardial infarctions and had severe mitral regurgitation due to papillary muscle dysfunction. Both had severe three-vessel coronary disease and were in Functional Class IV. Gratifying results were obtained in the remaining patients, all of whom had severe valvular disease and significant coronary artery occlusive disease.

Throughout our experience great emphasis has been placed on maintaining continuous and adequate coronary perfusion. Hypothermic anoxic cardiac arrest was not employed. When aortic cross-clamping was necessary, the aorta was opened and the coronary arteries were perfused through the coronary ostia. A dry field was maintained while the vein–coronary artery anastomosis was performed by occluding the artery immediately proximal and distal to the arteriotomy. Cross-clamping of the aorta was rarely employed. Though very satisfactory results have been reported with the use of hypothermic anoxic arrest [9], we believe that the maintenance of coronary perfusion with brief or no interruption is vitally important in the prevention of myocardial necrosis intraoperatively. By performing the aortocoronary bypass graft as the initial part of the operation, coronary perfusion is improved early in the operation and the period of ischemia is shortened. Of equal importance is the policy of grafting all major coronary vessels with significant obstruction. It has been our policy to graft any vessel with greater than 50% obstruction. An average of 2.5 grafts per patient was performed. It has not been demonstrated that the increase in operative time required for multiple grafts has impaired the operative results.

It is accepted that patients undergoing valve replacement who have coexisting coronary artery disease have a significantly higher operative mortality than patients free from coronary disease. It remains uncertain whether the addition of coronary artery bypass grafting in these patients actually decreases the operative mortality and improves long-term results. We believe, however, that coronary bypass grafting can be performed in conjunction with valve replacement without a significant increase in operative risk. By improving myocardial perfusion at the time of the valve operation, coronary bypass grafting may lower operative risk and improve late results in formerly high-risk patients. Severe coronary artery disease should not be a contraindication to valve operation.

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Comparison of Patients with Coronary Artery or Valve Disease: Intraoperative Differences in Blood Volume and Observations of Vasomotor Response

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ABSTRACT **A review of 296 patients undergoing cardiac operations has shown that those with coronary artery disease have a blood volume deficit. The 148 patients with valve disease had a normal blood volume of 78 ml/kg (normal range, 68–88 ml/kg), while the 148 with coronary artery disease had a blood volume of 69 ml/kg ($p < 0.001$). Infusion of plasma prior to cardiopulmonary bypass as well as the total transfusion required afterward to maintain blood pressure indicated an important clinical difference in these two groups. Another finding was that the requirement for a drug to control blood pressure prior to use of cardiopulmonary bypass was greater in the coronary patients ($p < 0.01$). Comparison of the requirement for a hypotensive agent before and after bypass showed a greater predictability in the valve group. This experience leads us to conclude that patients with coronary artery disease and angina not only have a low blood volume, but they also have a marked vasoactive lability which shows up in their hemodynamic response to the conduct of an operation and to anesthesia.**

Patients with coronary artery disease have been shown to have a lower than normal blood volume preoperatively [1, 3]. The deficit distinguishes these individuals when compared with other patients undergoing cardiac operations or with the normal population. This study was undertaken to determine how the preoperative blood volume deficit affects operative management of patients with coronary artery disease. From this analysis we postulate that these patients have a low blood volume, and as the byproduct of our observations we would suggest that they also have a different vasomotor response when compared with patients having valve disease. These observations help to explain the differences seen in the patients' hemodynamic response during the induction of anesthesia as well as the differences seen in transfusion requirements following discontinuation of cardiopulmonary bypass. The study is a compilation of our operating room experience, and it helps to define the different circulatory patterns in the two groups and provides data giving objectivity to our clinical observations.

Methods

The records of 296 patients who had cardiac operations during a two-year period (July, 1971, to August, 1973) were reviewed. The data shown in Table 1 were used to compare patients with the following diagnoses: aortic insufficiency, aortic stenosis, mitral regurgitation, mitral stenosis, and coronary artery disease (Table 2).

The patients were all managed according to a standard protocol that included measurement of blood volume on the day prior to operation using the radioiodinated serum albumin technique. In the operating room, management was standardized by adherence to predetermined criteria for both transfusion and use of hypotensive agents based upon the intraarterial blood pressure.

Intraoperative Management and Anesthetic Technique

Morphine sulfate (1 mg/kg) to induce anesthesia was administered intravenously in 3 to 6 mg

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Table 1. Data Analyzed by Computer to Study Differences between Patients with Coronary Artery Disease and Patients with Valve Disease

Diagnosis	Height
Age	Weight
Body surface area	
Congestive heart failure (history of)	
Left ventricular end-diastolic pressure	
Volume transfused following bypass	
Blood pressure	
Use of: morphine, N_2O, epinephrine, halothane, chlorpromazine, plasma infusion, curare, trimethaphan	

increments over a period of 15 to 20 minutes. As respiration became depressed, oxygen and nitrous oxide (3 liters/3 liters) were administered by mask and ventilation was controlled. If the patient was still responding to verbal stimuli after his last dose of morphine, diazepam, 5 to 15 mg, was given intravenously. Intubation was facilitated by the use of succinylcholine, 80 to 100 mg intravenously. Intermittent injections of curare were administered to maintain adequate relaxation throughout the operation.

Whenever extended, clinically significant hypotension developed prior to use of the heart-lung machine, the central venous pressure was assessed. If it was low or if the level had decreased from what it was prior to the induction of anesthesia, 250 to 500 ml of plasma protein fraction was infused intravenously. If the CVP was elevated, calcium chloride, 0.5 to 1 gm, or an infusion of epinephrine (8 μg/min) was administered to maintain the patient's blood pressure in his normal preoperative range.

Hypertension (diastolic pressure > 90 mm Hg) prior to the use of cardiopulmonary bypass was treated with halothane in concentrations sufficient to reduce the patient's blood pressure to the preoperative level. This agent was also used during bypass when the mean arterial pressure rose above 100 mm Hg. Following bypass, blood was transfused using left atrial pressure as a guide (maximum, 20 mm Hg). An attempt was made to maintain the blood pressure above 100 mm Hg with the widest possible pulse pressure. When this was not possible, the hypotension from myocardial weakness was treated with small doses of epinephrine. If a patient was hypertensive following bypass, treatment was given with chlorpromazine in a 1 to 2 mg bolus intravenously. If the hypertension was still uncontrolled after 8 mg of chlorpromazine had been given, an infusion of trimethaphan, 1 mg/ml, was started and administered at a rate sufficient to keep the diastolic blood pressure below 90 mm Hg.

Results

Blood Volume

Table 3 shows blood volume data for all patients in the study. When the patients were grouped into coronary vein graft (CVG) and valve replacement (VR) categories, CVG patients had significantly lower blood volumes than VR patients ($p < 0.001$). When a more detailed analysis was made by diagnosis, patients with aortic

Table 2. Comparison of Patients with Coronary Artery Disease and Patients with Valve Disease

Disease & Operation	No. of Patients	Age (yr)	BSA (m^2)	CHF[a]	LVEDP (mm Hg)
All CVG patients	148[b]	51	1.88	35	16
Only CVG	119	50	1.90	25	13
All VR patients	148[b]	49	1.76	81	16
Only MS	15	51	1.89	7	19
Only MR, MS, AI	121	49	1.74	65	16

[a] By history.

[b] Twelve patients had both valve replacement and coronary vein grafting. Seventeen patients had resection of left ventricular aneurysm and coronary vein grafting.

CVG = coronary vein graft; VR = valve replacement; MR = mitral regurgitation; MS = mitral stenosis; AI = aortic insufficiency.

Table 3. Blood Volume Data for Patients with Coronary Artery Disease or Valve Disease

Disease & Operation	Volume (ml/kg)		
	Plasma[a]	RBC[b]	Blood[c]
All CVG patients	41.0	29.4	70.4
Only CVG	40.0	29.4	69.4
All VR patients	45.2	31.0	76.2
Only AS	42.1	29.5	71.6
Only MR, MS, AI	47.1	31.1	78.2

[a] Normal range, 39–49 ml/kg.
[b] Normal range, 30–38 ml/kg.
[c] Normal range, 68–88 ml/kg.
Abbreviations same as in Table 1.

stenosis were seen to act more like CVG patients with respect to blood volume, and there was no significant difference between the CVG and AS groups.

Transfusion

During induction of anesthesia, infusion of plasma was required in 69 of 119 patients who had CVG only versus 31 of 121 patients who had VR only ($p < 0.001$) (Table 4). Transfusion after bypass was also greatest in CVG patients ($p < 0.05$) (Table 4).

Hypotensive Agents

At the time the skin incision was made, blood pressure rose to higher than 150 mm Hg systolic or 90 diastolic in 77 of 119 CVG patients versus 45 of 121 of the VR group ($p > 0.01$). These are the patients in Table 4 who required halothane. It is noteworthy that the aortic stenosis patients differed from the other patients in the VR group in that they had a blood pressure rise in 7 of 15 cases. Following cardiopulmonary bypass, chlorpromazine was required to lower blood pressure in 52 of the CVG patients and 25 of those having VR ($p > 0.01$). Patients with aortic stenosis again were more like those with coronary disease in that 6 of them required chlorpromazine for control of hypertension.

The predictive nature of hypertension before bypass with respect to the requirement for hypotensive agents after bypass was investigated. In the CVG groups there were 42 patients (35%) in whom no halothane was necessary prior to bypass. Eighteen of these 42 (42%) required chlorpromazine after bypass. In the valve replacement group, however, there were 76 (63%) who needed no hypotensive agent before bypass, and only 7 (9%) of these needed chlorpromazine afterward.

Comment

The results of this analysis strongly support previous work by others showing that blood volume is lower in surgical patients with coronary artery disease [1, 3]. This deficit is the reason that CVG patients require additional volume during induction of anesthesia, particularly when agents which decrease vasomotor tone are used. This is illustrated by the increased need for plasma, presumably resulting from the routine use of morphine. The requirement for more transfusion when bypass is discontinued may also be explained by the low blood volume in these patients.

There is, however, a seeming paradox in the CVG patients because they may subsequently require vasodilation to treat hypertension. This strongly suggests that there are two factors responsible for the labile hemodynamic course of such patients: low blood volume and increased

Table 4. Comparison of Use of Transfusion and Use of Hypotensive Agents in Patients with Coronary Artery Disease and Patients with Valve Disease

Operation	Transfusion During Induction	Transfusion After Bypass (ml)	Hypotensive Agent	
			Halothane	Chlorpromazine
Only CVG	58%	2,469	65%	44%
Only MR, MS, AI	26%	2,089	37%	21%

Abbreviations same as in Table 1.

vasomotor tone. Some patients in the valve replacement group needed control of their acutely elevated blood pressure, which indicates that this group can also show increased vasoactivity; but the number is significantly less and is not associated with a low blood volume.

Morgan and associates [4] have shown that these two groups of patients have similar abnormalities in vasomotor tone during their early postoperative recovery to those we have depicted. He compared patients having coronary grafting with those receiving valves and showed that increased peripheral vascular resistance is present longer and to a greater degree in the patients undergoing vein grafting.

Predicting patients who might prove to be hypertensive in the early postoperative period on the basis of their blood pressure prior to bypass was not possible in the CVG group because 42% of the patients who had no significant blood pressure rise in response to this stimulus had enough hypertension after bypass to require vasodilation. In the valve group, only 9% who received no treatment before bypass needed it afterward. This is interpreted as supporting the conclusion that CVG patients have increased vasomotor activity that may manifest itself at any time before, after, or during bypass. The unpredictability is characteristic of CVG patients.

A new and interesting finding of this study is that patients having aortic valve replacement for stenosis resemble CVG patients with respect to both blood volume and requirements for hypotensive agents more than they resemble patients undergoing replacement of other valves. It is not possible to speculate about a common mechanism for this similarity, but both categories have high left ventricular pressure in common, the former because of valve obstruction and the latter due to myocardial ischemia and angina [2]. Further investigation may clarify the mechanisms involved, but in the absence of more precise knowledge it seems proper to accept the results of this analysis as an indication of the increased risks in patients with coronary artery disease and aortic stenosis, not only during cardiac operations, but during any procedure requiring anesthesia. The possibility of unmasking their inherent hypovolemia by removing the vasoconstriction which seems to support their circulation must be anticipated and promptly treated with volume expansion. It also must be recognized that subsequently these patients may have a higher than normal blood pressure and may require vasodilation to maintain adequate perfusion.

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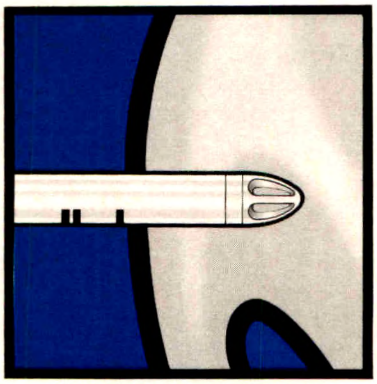

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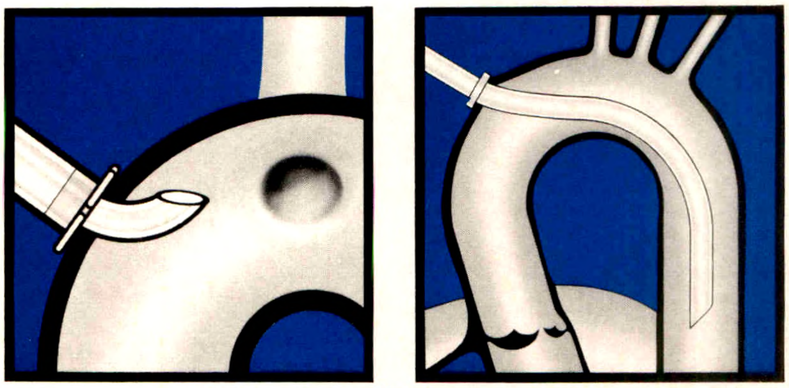

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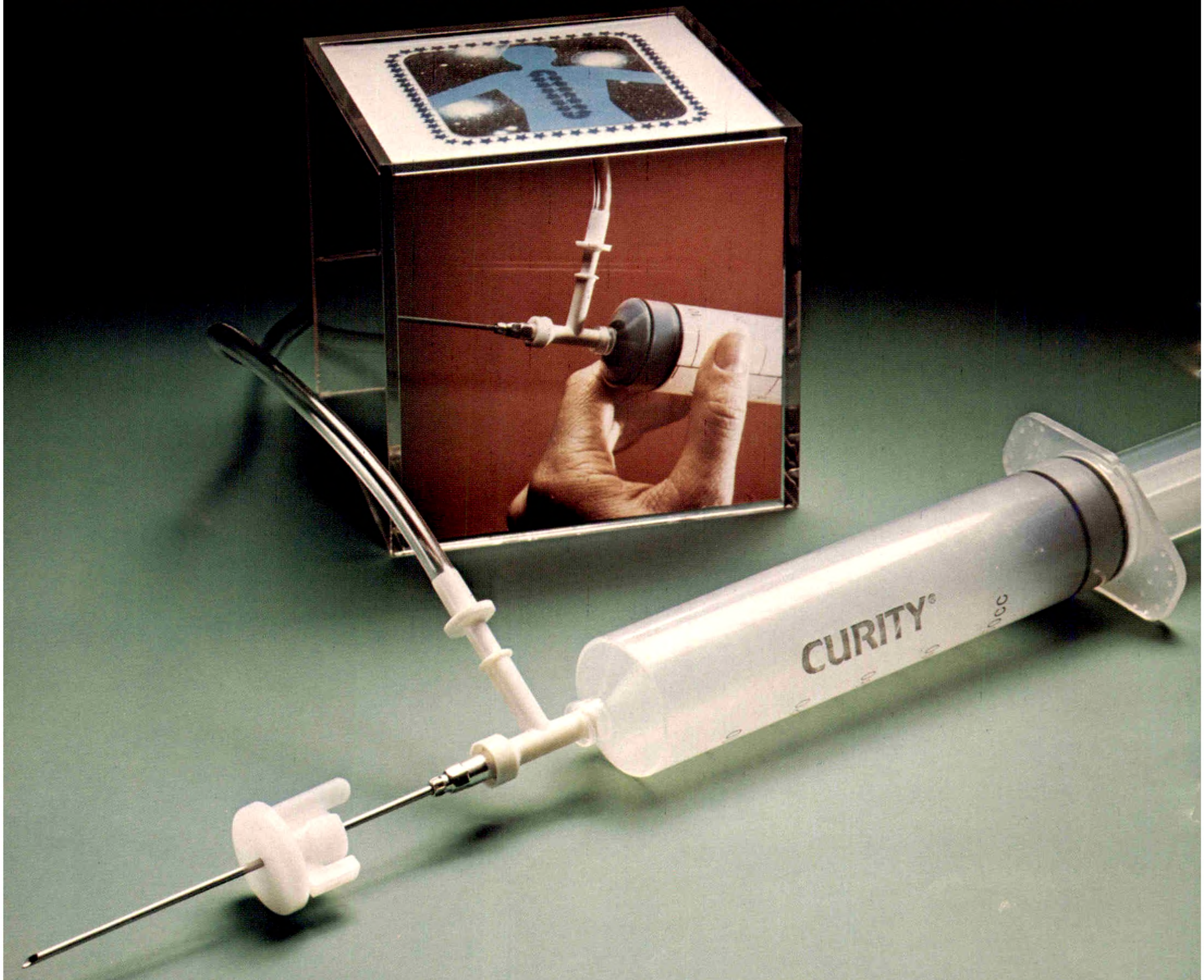

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Constant-Pressure Coronary Artery Perfusion during Aortic Valve Operations

Stanley Giannelli, Jr., M.D., Edward F. Conklin, M.D., Robert T. Potter, M.D.,
Enrique A. Bonfils-Roberts, M.D., James T. Mazzara, M.D.,
and Augusto H. Moreno, M.D.

ABSTRACT **We considered the theoretical differences between the normal relationships of coronary blood flow and perfusion pressure in the working heart and those obtained with continuous, steady-flow perfusion by a roller pump during aortic valve replacement. Steady pump perfusion should deliver less blood flow to the endocardium because:**

1. **For the same mean artery perfusion pressure, the average coronary blood flow is less with constant-flow pump perfusion.**
2. **With constant pump perfusion, pressure would be excessively high during systole, and during diastole it would be significantly lower than the mean perfusion pressure.**

Instantaneous pressure and flow were measured in the left coronary artery in 8 patients undergoing aortic valve replacement, employing either roller pump perfusion or a gravity flow system to provide a steady pressure source. Although we did not attempt to demonstrate improved endocardial flow, the mean left coronary flow was always greater with gravity perfusion (297 versus 153 ml/min), lending support to the theoretically proposed differences between the two perfusion methods.

Theoretically, continuous coronary perfusion should be the most physiological method of providing adequate myocardial oxygenation during aortic valve replacement. Since oxygen requirements are considered to be continuously satisfied, progressive myocardial hypoxia would not be expected to occur. This contrasts with those methods which do not employ coronary perfusion but instead reduce myocardial oxygen requirements, either by hypothermia or by flushing the coronary circulation with a metabolic inhibitor. These methods impose a time limitation, because myocardial oxygen consumption is not totally eliminated and the lactic acid produced by anaerobic metabolism is not removed.

Despite the apparent soundness of the concept of continuous coronary artery perfusion, patients so managed occasionally suffer impaired left ventricular function after aortic valve replacement. While the most common form of dysfunction is expressed by a transient requirement for inotropic support after heart-lung bypass, some patients, usually those with severe left ventricular hypertrophy, cannot be weaned from bypass by any means. The usual postmortem finding in these patients, or in those who die in the early postoperative period, is subendocardial ischemic necrosis [2].

Buckberg and his associates [1] have made important contributions to our understanding of those factors determining the adequacy of endocardial blood flow during continuous coronary perfusion. They emphasized that the heart should not be allowed to fibrillate, because intramyocardial tension in the inner zones may then constantly exceed perfusion pressure, causing endocardial ischemia, especially in the hypertrophied left ventricle. They have also stressed that pressure at the coronary ostia must be adequate, in the 90 to 100 torr range; therefore the pressure drop across the perfusion tubing, from the point of pressure measurement to the coronary ostium, must be known for each flow rate.

Despite our careful adherence to these two principles, some of our patients continued to suffer left ventricular damage. Usually this was mild, but the last patient so managed developed the so-called stone heart. This led us to examine

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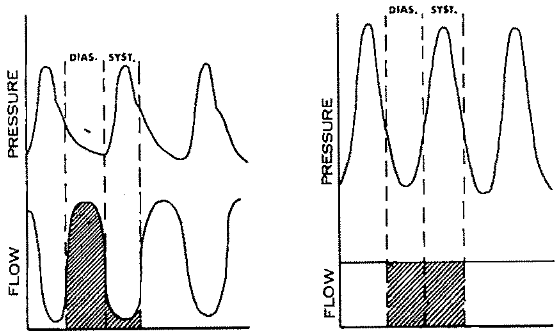
the implications of the differences between the normal pattern of coronary perfusion in the working heart and continuous coronary perfusion with roller pumps in the empty, beating heart.

The left panel of Figure 1 presents the normal coronary pressure-flow relationship in the working heart. Even in the nonhypertrophied heart almost all flow occurs during diastole, because although pressure is higher during systole, the corresponding increase in intramyocardial tension constricts the coronary vasculature. Thus coronary flow is dependent upon the relationship between diastolic perfusion pressure and diastolic coronary vascular resistance.

If myocardial wall tension also increases significantly during systole in the beating, non-working heart, it can be theoretically demonstrated that continuous perfusion of the coronary arteries at a constant rate throughout the cardiac cycle has several undesirable effects:

1. Blood flow to the endocardial zone becomes a smaller percentage of total coronary flow. The right panel of Figure 1 diagrams the situation that obtains with steady, continuous coronary perfusion. Approximately one-half of total flow occurs during systole, and to the extent that systolic wall tension is increased, this systolic flow preferentially goes to the epicardial rather than to the endocardial zone. Thus a lesser percentage of total coronary flow is available to the endocardium.
2. Coronary systolic pressure oscillations may be dangerously high. During systole, coronary perfusion pressures are elevated above the desired mean perfusion pressure and, if sufficiently elevated, could damage the coronary vasculature. Conversely, to the extent that the systolic pressure is elevated above the mean pressure level, diastolic coronary perfusion pressure is correspondingly less and might not be sufficient to deliver blood to the endocardium.
3. At any mean level of coronary artery perfusion pressure, total coronary blood flow throughout a complete cardiac cycle is less when continuous perfusion is provided at a steady rate by a pump than it is when the flow is obtained during the normal, phasic pattern of coronary flow.

Fig 1. Differences between the normal pattern of coronary blood flow in the normal working heart and the coronary perfusion pattern obtained during aortic valve replacement with circulation maintained by roller pumps.



NORMAL PATTERN OF CORONARY FLOW

PUMP PERFUSION OF CORONARY ARTERY

The usual arrangement of the equation describing the steady-state relationship between flow, resistance, and pressure is based upon the electrical analogy of Ohm's law:

$$\text{Flow} = \text{pressure}/\text{resistance} \quad (1)$$

which, transposed, becomes:

$$\text{Pressure} = \text{flow} \times \text{resistance} \quad (2)$$

When the coronary arteries are individually perfused with roller pumps, the rate of perfusion is generally set so as to achieve the desired mean coronary perfusion pressure. If the resistance of the coronary perfusion tubing and cannula is known, coronary ostial pressure can then be calculated for each flow rate.

In order to achieve the greatest possible flow at any level of mean perfusion pressure, the flow factor rather than the resistance factor in Equation 2 should be maximized. Thus the delivery of flow should be increased during diastole to match the decrease in vascular resistance, and conversely, flow should be decreased during systole.

Figure 2 plots the simultaneous flow and pressure values from Equation 2 that generate a pressure of 100 torr. Ideal adherence to the principle of maintaining a constant coronary perfusion pressure would require that coronary flow be continuously varied to accommodate to the changing coronary vascular resistance according to this flow-resistance plot.

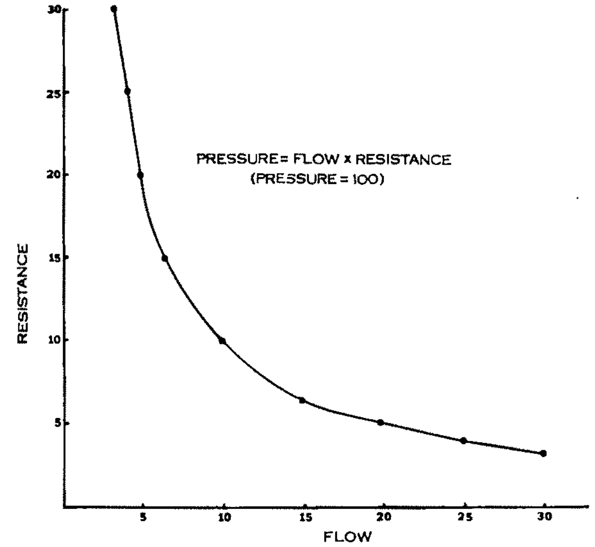


Fig 2. Plot of simultaneous values for flow and resistance from Equation 2 (see text) that produce a pressure of 100 torr.

It can easily be demonstrated that if the desired mean perfusion pressure is exceeded by an inappropriately high perfusion rate during the high-resistance phase of the cardiac cycle, then there must be a greater decrease in the flow rate during the low-resistance phase of the cycle in order to achieve the desired mean pressure over the entire cycle. Thus the mean perfusion rate required to achieve the same perfusion pressure during a cardiac cycle would be less with a steady perfusion rate than when coronary flow is phasic in accordance with the resistance-flow relationship of Equation 2 and Figure 2.

Figure 3 plots the flow pressure and resistance relationships during a hypothetical cardiac cycle. The desired mean perfusion pressure is 100 units, and resistance varies from 100 to 10 units. When flow is phasic and is matched to resistance according to the plot of Figure 2, the mean flow during the cardiac cycle is 2.54 units compared with 1.74 units when steady perfusion is employed. While perfusion pressure is steady at 100 units when phasic flow is employed, it varies from 174 to 17.4 units when steady flow is used. The method of generating the plots in Figure 3 is presented in the Table.

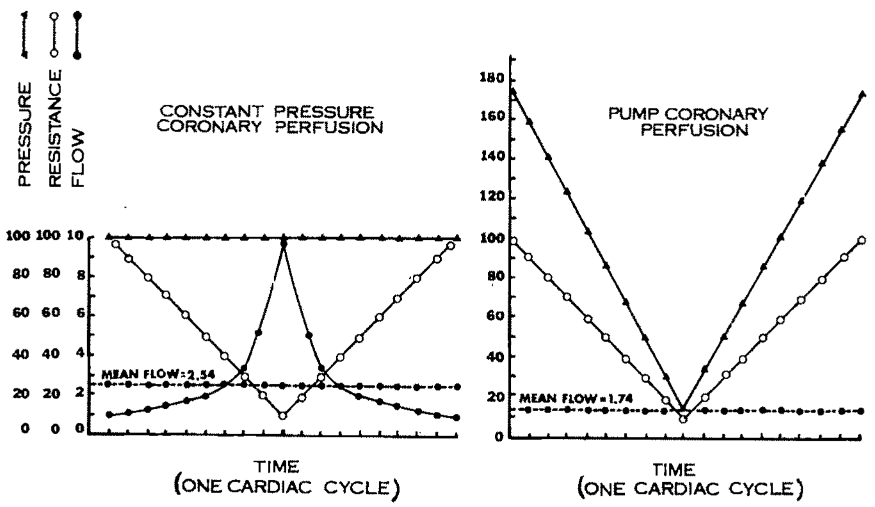
There is no feasible method of constantly changing coronary blood flow in response to variations in coronary vascular resistance. Instead, we have chosen to evaluate the feasibility of fixing the coronary pressure level by providing a steady pressure source with a reservoir gravity-feed system, thus allowing the coronary vascular bed to automatically regulate flow in response to alterations in resistance.

The theoretical analysis represented in Figures 1 and 3 assumes that the coronary perfusion tubing and the coronary vasculature are totally noncompliant. To the extent that there is distensibility in this combined system, some of the blood pumped during systole would be stored in the tubing and vessels and then would be delivered during diastole, thus ameliorating the deleterious effects of steady pump perfusion.

Methods

Eight patients undergoing either aortic or aortic and mitral valve replacement were evaluated.

Fig 3. Flow and pressure relationships plotted for a hypothetical cardiac cycle under conditions of steady-flow and steady-pressure perfusion.



Resistance, Flow, and Pressure Values in Hypothetical Cardiac Cycles Employing Constant Pressure and Constant Flow

Constant-Pressure Perfusion			Constant-Flow Perfusion		
R	F	P	R	F	P
100	1.0	100	100	1.74	174.3
90	1.1	100	90	1.74	156.9
80	1.25	100	80	1.74	139.5
70	1.42	100	70	1.74	122.0
60	1.66	100	60	1.74	104.6
50	2.0	100	50	1.74	87.2
40	2.50	100	40	1.74	69.7
30	3.30	100	30	1.74	52.3
20	5.0	100	20	1.74	34.9
10	10.0	100	10	1.74	17.4
20	5.0	100	20	1.74	34.9
30	3.30	100	30	1.74	52.3
40	2.50	100	40	1.74	69.7
50	2.0	100	50	1.74	87.2
60	1.66	100	60	1.74	104.6
70	1.42	100	70	1.74	122.0
80	1.25	100	80	1.74	139.5
90	1.1	100	90	1.74	156.9
100	1.0	100	100	1.74	174.3
Σ 1,090	48.52	1,900	Σ 1,090	33.1	1,900

[a] Figure 3 was plotted from the numbers above, which were generated from a hypothetical cardiac cycle in which resistance varied in increments and decrements of 10 units from a peak of 100 units in systole to a low of 10 in diastole. The mean pressure level is 100 units.

The three left columns represent the sequential flow rates necessary to generate 100 pressure units according to the equation Pressure = flow × resistance. The average flow during the cardiac cycle is 2.54 units and ranges from 1.0 at peak systole to 10 in diastole, when the vascular resistance is least.

The numbers in the three right columns were generated by determining the steady, mean flow rate that would generate a mean pressure of 100 units.

$100 = F \times 1{,}090$
$F = 1{,}900/1{,}090$
$F = 1.74$ units

This was then multiplied by each resistance unit to determine the pressure level generated in each interval.
R = resistance; F = flow; P = pressure.

They were perfused with roller pumps, and gas exchange was obtained with either a bubble or a membrane oxygenator. The perfusate temperature for both the coronary and systemic circulations was 30°C. The extracorporeal circuit prime consisted of 4 units of packed red cells whose buffy coat had been removed, 1,000 ml of 5% albumin solution, and 2 liters of normal saline.

A silicone rubber, bulb-tipped cannula was placed in the left coronary ostium and fixed with a suture (Fig 4). When possible, the right coronary artery was similarly cannulated. Measurements were not made of right coronary flow. The right coronary artery was continuously perfused by a roller pump at a mean ostial pressure of 90 to 100 torr.

The left coronary artery was perfused by one of two methods:

1. An occlusive roller pump accommodating Silastic tubing with an internal diameter of 6 mm delivered 8 ml per complete revolution. The distance from pump to coronary ostium was 1.8 m. The compliance of this circuit was determined by filling a similar length of tubing with saline to a static pressure of 100 torr.

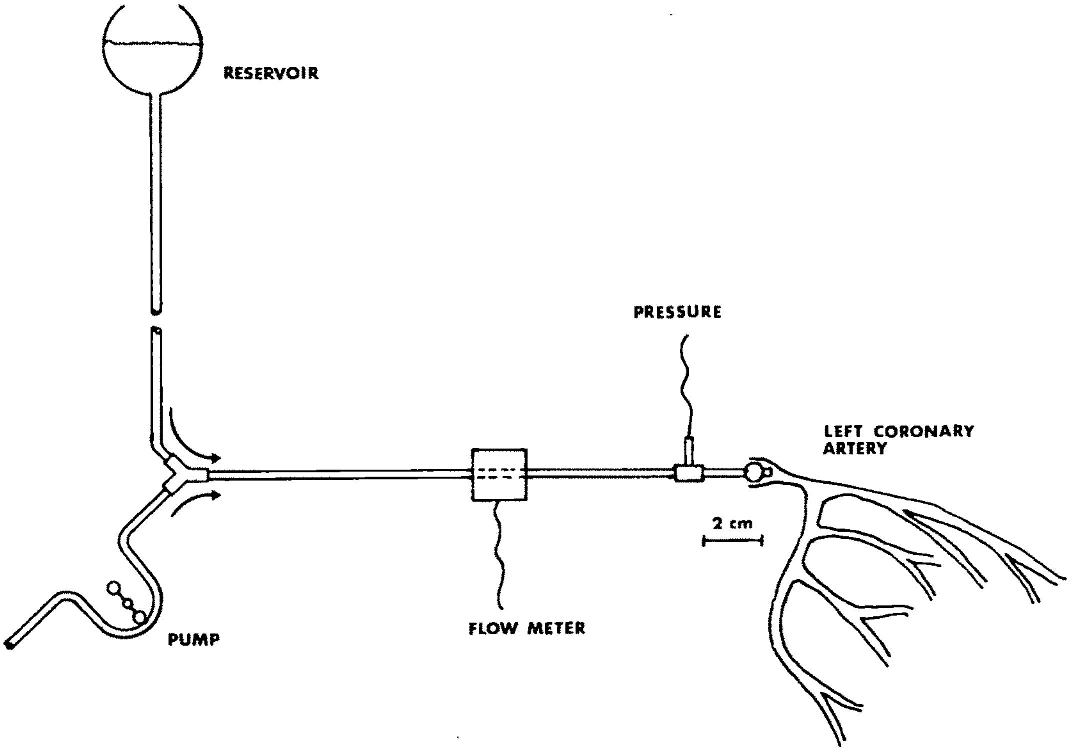


Fig 4. The experimental arrangement, which was designed to provide either continuous pressure or continuous flow perfusion of the left coronary artery.

The addition of 0.4 ml of saline then raised the static pressure to 140 torr.

2. Flow was delivered by gravity through similar 6 mm internal diameter tubing from a reservoir suspended from a pole of adjustable height, which joined the line from the pump 10 cm beyond the pump head. A flow probe was placed in the line 20 cm from the coronary ostium. Pressure was obtained directly from the coronary cannula 2 to 3 cm from the ostium. At a flow of 600 ml/min the pressure drop across the distal portion of the cannula, beyond the point of pressure measurement, was 6 to 8 torr.

The reservoir height was adjusted to obtain the desired ostial perfusion pressure. Greater reservoir height was required for higher left coronary flow because of the resistance of the perfusion tubing. The usual vertical distance between reservoir level and coronary ostium was 180 to 200 cm. Employing this hydrostatic pressure, 800 ml/min of perfusate flowed freely from the coronary perfusion cannula into a beaker. When flow was delivered through either the pump or the gravity system, the tubing to the other source was clamped next to the Y-connector.

Simultaneous left coronary flow and pressure measurements were made upon the beating heart at the same mean perfusion pressures, 90 to 100 torr, during coronary perfusion by either pump or gravity. In the first 2 patients gravity flow was employed only during measurements. In the remaining 6 patients, gravity perfusion of the left coronary artery was employed during the entire procedure, except for the brief intervals when measurements were made during pump perfusion.

Mean coronary flow rate could be independently determined from the flowmeter and from the rpm of the occlusive coronary roller pump, or by timing the outflow from the graduated gravity reservoir. The flowmeter readings were within 5 to 10% of the flow rates measured directly from the pump or reservoir.

Results

There were no hospital deaths, and inotropic drugs were not administered either at the end of bypass or later postoperatively.

During pump perfusion of the left coronary artery, pulsations were transmitted to the left coronary artery system and to the perfusion tubing by the increased vascular resistance during systole (Fig 5). The corresponding flow pattern was always phasic, with the greater flow occurring during diastole due to the interactions between the increased systolic coronary vascular resistance and the distensibility of the coronary perfusion tubing. The latter converted the steady output of the perfusion pump to a phasic coronary flow pattern.

When the left coronary artery was perfused by gravity and thus allowed to automatically regulate to variations in vascular resistance, the flow pattern again was phasic. There usually was a greater disparity between systolic and diastolic flow with gravity than with pump perfusion, and the nature of the flow pattern was variable. Occasionally there was complete cessation of systolic flow. Usually this was intermittent and was related to the increased force of ventricular contraction associated with postextrasystolic contractions (Fig 6); however, there were several instances of almost complete systolic flow interruption during sustained periods of regular rhythm (Fig 7).

The phasic variations in perfusion pressure with gravity flow were probably caused by the resistance in the coronary perfusion tubing system. Most of the resistance was in the terminal silicone rubber cannula, proximal to the point of pressure measurement. As noted in Methods, the maximum expected pressure drop from the point of pressure measurement to the coronary ostium was 6 to 8 torr. There was relatively little resistance in the 6 mm internal diameter tubing. When systolic ventricular contraction compressed the coronary vasculature and thus reduced flow, the resistance-induced pressure drop across the perfusion system also decreased and coronary perfusion pressure increased, approaching the static hydrostatic pressure generated by the column of perfusate from the level in the reservoir to the coronary ostium. (With complete cessation of flow, ostial pressure equals the total static hydrostatic pressure of the perfusate column.)

When the mean perfusion pressure was maintained constant at a level between 90 and 100 torr and flow was abruptly changed from one method to the other, the total flow during gravity perfusion was always greater than with steady pump coronary perfusion.

The flow rates for each coronary perfusion method tended to remain constant for each of the 8 patients during the entire operation. Figure 8 presents mean left coronary blood flow for

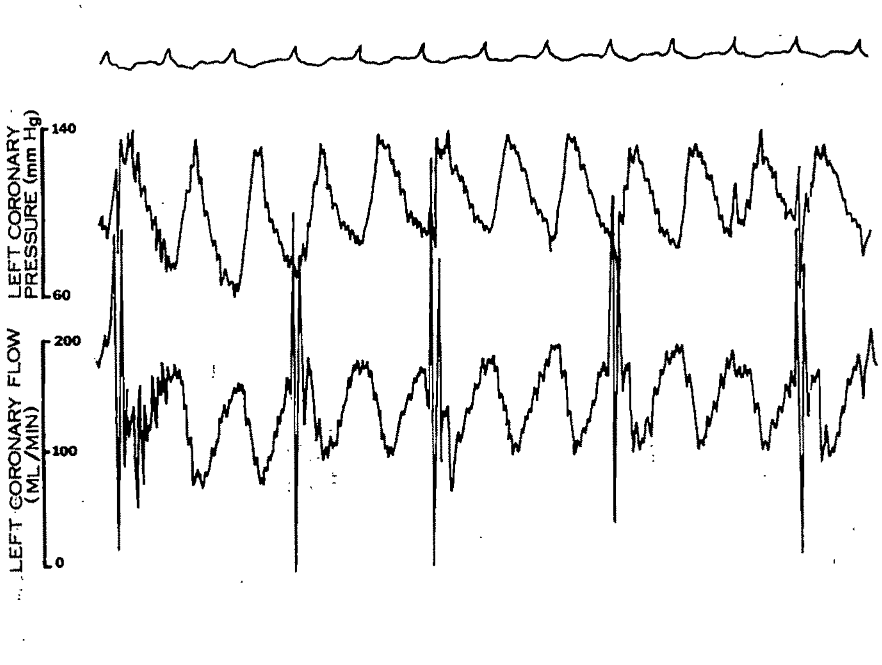


Fig 5. Representative tracing of flow and pressure during roller pump perfusion of the left coronary artery. The pressure is phasic because of increased systolic vascular resistance. During systole some of the flow delivered from the pump is stored in the tubing, to be delivered to the coronary artery during diastole. Thus the steady output of the pump is converted to phasic coronary flow by the distensibility of the tubing. The widened, frequent pressure oscillations represent the point at which the roller engages the tubing in the pump head.

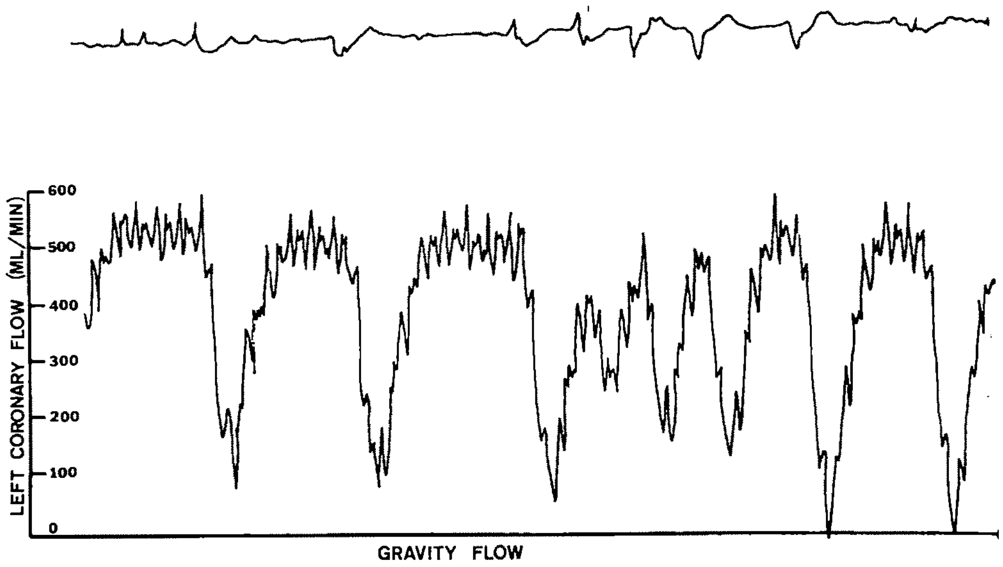


Fig 6. Representative left coronary flow tracing during gravity perfusion. The extent of systolic flow interruption is related to the force of ventricular contraction, which varies with the cardiac rhythm.

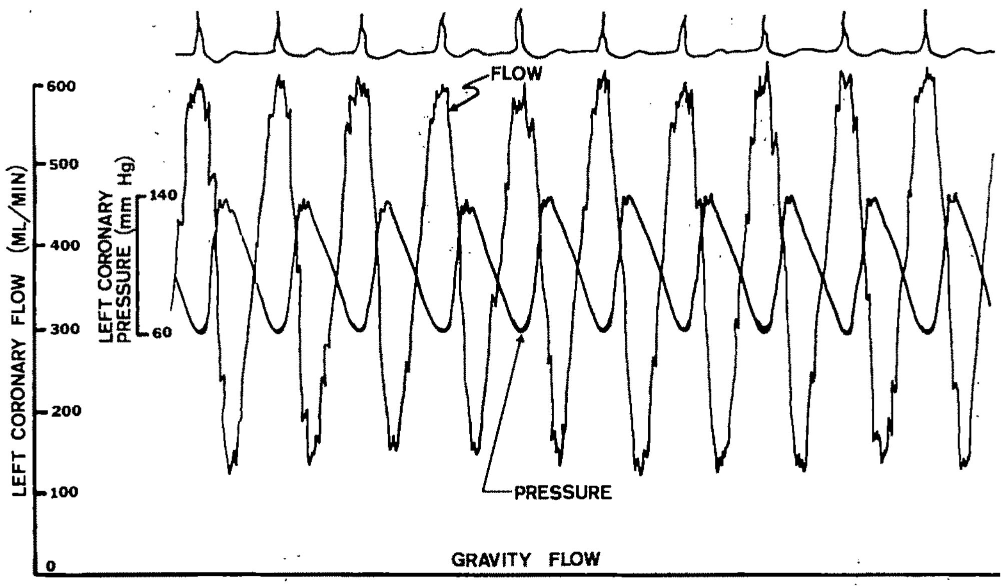
each patient, measured during the change from one to the other form of coronary perfusion.

The average flow during pump perfusion for the entire group was 153 ml/min and was 297 ml/min during gravity perfusion. The greatest percentage increase was from 100 to 300 ml/min. The greatest absolute mean flow rates were in 2 patients who had 410 and 395 ml/min, respectively, during gravity perfusion. Peak diastolic flow rates of 600 ml/min were achieved in several patients.

Comment

These data do not prove that endocardial blood flow is improved by gravity perfusion of the coronary arteries. However, they strongly suggest that this does occur, because mean coronary perfusion was always higher during gravity perfusion, thus lending support to the theoretical analyses of the two perfusion methods. This improvement in mean coronary flow occurred despite the fact that the coronary

Fig 7. Tracing of a stable left coronary pressure and flow pattern during gravity perfusion. Pressure is phasic, despite the constant pressure source, because the resistance of the coronary perfusion cannula imposes an increased pressure drop along its length with greater coronary flow.



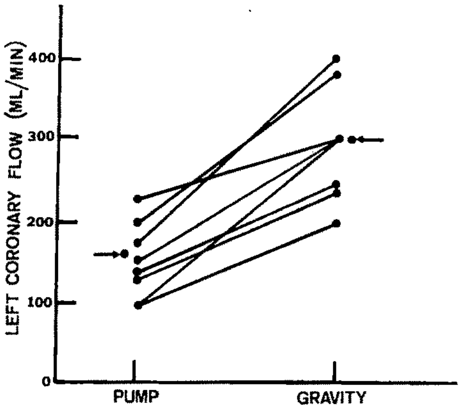


Fig 8. Mean coronary flows for each patient under conditions of gravity and pump perfusion of the left coronary artery.

perfusion tubing was sufficiently compliant to convert the steady output of the pump to phasic flow. Had the tubing been less compliant, the average flow during pump perfusion probably would have been further reduced at the same mean perfusion pressure.

These data suggest that variability in the distensibility of perfusion tubing may contribute to differences in morbidity and mortality between surgical groups who otherwise adhere to the same coronary perfusion protocol. A distensible bladder inserted into the coronary perfusion tubing distal to the pump would be expected to approximate the results obtained with gravity perfusion.

The use of larger diameter coronary cannulas that taper near the ostium would achieve better flow responses to variations in resistance when a constant pressure source is employed. The differences in the increments of flow between the two perfusion methods in different subjects was related to intrinsic differences in left ventricular configuration, which we did not assess. Since the difference in flows between the two methods remained quite constant in each patient during the course of the operation, it is unlikely that inotropic stimuli were responsible for the differences between patients, because these would have been expected to vary with time in each patient.

Experiments measuring endocardial blood flow and metabolism in animals with surgically induced left ventricular hypertrophy are clearly indicated. If constant-pressure perfusion enhances endocardial oxygenation, then this method should be employed in those clinical studies comparing coronary perfusion with other methods of myocardial support, such as hypothermia and metabolic inhibition.

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Discussion

DR. S. R. K. IYENGAR* (Kingston, Ont, Canada): I wish to congratulate Dr. Giannelli for focusing our attention on the need for a critical analysis of our conventional perfusion techniques. Gravity perfusion, which we have used for five years, is a sound concept. The primary problem with coronary perfusion is one of distribution and not one of volume of flow.

When the perfusion pressure is increased from 40 mm Hg there is a rise in intramyocardial pressure and oxygen consumption and a decrease in subendocardial flow. Therefore I raise the following three fundamental questions: Should not the ideal perfusion pressure be around 40 to 50 mm Hg? Should not the heart be arrested during perfusion to eliminate intramyocardial pressure gradients and maintain constant coronary vascular resistance to allow even distribution? And is blood the ideal perfusate for coronary perfusion?

We have found it quite logical, simple, and effective to modify the perfusate in order to meet the criteria of satisfactory perfusion. Over the past five years we have evaluated coronary perfusion in rabbits, dogs, and humans using a colorless substitute for blood. It has no red cells or platelets and it contains 12 mEq of potassium as well as glucose, insulin, and low-molecular-weight dextran.

There is ample evidence from our laboratory and other investigators that an arrested heart can derive adequate energy to meet its metabolic needs through glycolytic pathways in the absence of oxygen. The perfusate is colorless, and the low viscosity permits intermittent low-volume, low-pressure perfusion under gravity flow. The average flow per minute is about 15 ml, and the perfusion pressure is approximately 50 mm Hg. It has proved effective in both dogs and humans during anoxic arrest up to two hours.

Our experimental studies have revealed that after two hours of anoxic cardiac arrest (without perfusion), the heart attains the state of the so-called stone heart. Angiography in these hearts reveals no subendocardial vascular filling; also, the pH drops to 6. With bloodless coronary perfusion during two hours or more of anoxic arrest, the pH remains around 6.8 to 7.1, and there is good recovery of myocardial function with return of stable, normal blood pressure, regular sinus rhythm, and a good ejection fraction. Angiographic studies have revealed excellent filling of subendocardial vessels, and the myocardium has failed to show any ischemic contracture.

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*Deceased.

In conclusion, it has been our experience that the major problems associated with coronary artery perfusion can be overcome using a colorless perfusate which has low viscosity and provides adequate substrate anaerobic metabolism. We have used this technique during open-heart operations for more than five years without problems.

DR. STEPHEN Z. TURNEY (Baltimore, MD): The maintenance of a high stable coronary perfusion pressure, taking into account the gradient across the cannula and the hematocrit and temperature effects on blood viscosity, is crucial in any technique of coronary perfusion. I have recently used a somewhat different approach to coronary perfusion in a variety of cardiac procedures in adults.

The technique consists of cannulating the ventral aortic root proximal to a cross-clamp using a 10 or 12F Bardic cannula. A nominal coronary flow rate of 3 ml/kg/min promptly closes the aortic valve, and perfusion pressure is kept higher than 90 mm Hg. With the perfusate (ordinary hemodiluted pump prime) at 10°C or less, hypothermic cardiac arrest occurs very promptly, and within 8 to 10 minutes the myocardial temperature drops to the perfusate temperature even in a hypertrophied heart with coronary vascular disease.

If the aortic valve is insufficient, cavitary lavage through the valve assists in the cooling. The cannula may then be removed, and the heart is maintained at 10°C as measured by an intracavitary thermistor. This is accomplished by trickling the coronary perfusate over the surface of the heart. Arrest times of up to 45 minutes have been used clinically without ill effect, and longer periods are planned.

The technique is termed cryocardium by transaortic perfusion, abbreviated CTAP. Its advantages include hypothermic arrest prior to aortotomy in the case of aortic valve procedures or without aortotomy in other procedures. There is no anoxia and no need to use drugs or to fibrillate the heart while maintaining it thorough selective cooling of the myocardium at optimal perfusion pressures. Myocardial preservation after the periods of coronary perfusion is assured, cardioplegia persists even during reperfusion, and there is no damage to the coronary ostia with direct coronary ostial cannulation.

The aortic cannulation site may be used for subsequent anastomosis, as in coronary bypass grafting, or as a point on the aortotomy during aortic valve operations.

DR. LEWIS H. BOSHER (Richmond, VA): We have been interested in the problems and techniques of coronary perfusion for some time and use it when the local situation permits.

I thoroughly endorse the basic concept which Dr. Giannelli has expressed. Since 1962 we have used a technique of pressure-controlled automatic coronary perfusion. The system automatically and almost instantaneously adjusts flow rates in response to alterations in coronary vascular resistance. The apparatus consists of individual occlusive pumps that have control chambers with flexible diaphragms and a linear transducer that automatically regulates the flow according to preselected pressure.

We have used a pressure corresponding to a coronary ostium pressure between 90 and 100 mm Hg. The pressure is thus preset, and the flow varies. There is immediate recognition and response to obstructed coronary cannulas or catheters. Dangers of air embolism are eliminated. Priming volume is minimal, and the apparatus has proved remarkably durable and reliable. It has a sensitive response to metabolic oxygen debt, and vasodilatation has always been noted by temporary acceleration of flow, the pressure remaining constant.

The heart has been maintained in a beating state whenever possible, but the distribution of flow between subepicardial and subendocardial regions during systole and diastole has not been studied. I believe that the restrictive effect of systole on subendocardial flow is considerably lessened in the empty, beating heart compared with the full, beating heart.

I think Dr. Giannelli has made a very interesting and important contribution. In our own system I think we need to study phasic flow in the coronary perfusion line during systole and diastole, and we will certainly plan to do that. Our system has been particularly useful in reperfusion of the myocardium after distal anastomosis, when we have completed bypass of a critical obstruction and wish to reperfuse the ischemic heart as early as possible; and also when it is important to get some idea of the runoff at an early stage in the reconstruction.

DR. GIANNELLI: I thank the discussants. We did not mean to imply that coronary artery perfusion is the best method of myocardial preservation. However, I do think that the distribution of endocardial blood flow should be studied in an animal model with a hypertrophied left ventricle. If endocardial flow is in fact shown to be improved with a pressure-controlled rather than a flow-controlled system, then the former method should be applied to those clinical studies comparing coronary perfusion with other methods of myocardial preservation, such as hypothermia and metabolic inhibition.

Method of Managing the Small Aortic Annulus during Valve Replacement

Richard H. Blank, M.D., Dennis F. Pupello, M.D., Luis N. Bessone, M.D.,
Eric E. Harrison, M.D., and Sheldon Sbar, M.D.

ABSTRACT **In a series of 130 patients undergoing aortic valve replacement, 20 had the ascending aorta enlarged with a Dacron patch. Eight of these required division of the annulus with extension of the incision inferiorly to the anterior leaflet of the mitral valve. The resulting separation of the annulus allowed a larger size valve to be inserted. Glutaraldehyde-fixed porcine heterografts were used in all patients having the annulus enlarged. No deaths occurred in those patients having annular enlargement, and the postoperative studies show no evidence of mitral valve dysfunction.**

Replacement of the aortic valve in the presence of a normal or large aortic root can be accomplished with ease and safety in most instances [1, 2, 12]. The presence of a diminutive annulus, however, remains a problem in that both mechanical prostheses and stent-mounted tissue valves have significant resting gradients in the smaller sizes [3, 9]. In addition, a recent report [4] suggests that use of the small tilting-disc valve (Björk-Shiley) predisposes to thrombotic complications.

Based on encouraging follow-up studies of the Hancock glutaraldehyde-stabilized porcine heterograft [13], we have used this prosthesis in patients having an annular diameter less than 25 mm. In those instances when the annulus was too small to accept a prosthesis of adequate size, a technique has been used to allow expansion of the annulus, thereby permitting insertion of the next larger size valve. This report presents our experience in managing the small aortic root.

Clinical Material and Technique

One hundred thirty patients underwent aortic valve replacement during the period from July, 1972, through September, 1975. Twenty patients had enlargement of the ascending aorta using an appropriately tailored Dacron patch. In 8 of them the aortic root was small, necessitating enlargement of the aortic annulus by the technique to be described. There were 7 women and 1 man. Six patients had aortic stenosis and 2 had aortic insufficiency. Preoperative and postoperative catheterization data are summarized in the Table. The estimated aortic annulus diameter in this group ranged from 18 to 21 mm.

The heart was exposed through a midline sternotomy, and standard cannulation techniques were used. Moderate systemic hypothermia combined with perfusion at a relatively low flow rate was employed. Myocardial protection was provided by profound local hypothermia using a continuous cold saline irrigation of the pericardial well. Once stable perfusion was achieved, the aorta was cross-clamped and opened transversely and the incision was extended inferiorly into the noncoronary sinus. The aortic leaflets were resected, and all calcific deposits were carefully removed. The interior of the heart was irrigated with cold saline as the annulus was measured.

For those patients whose aortic root was deemed too small to accept a valve of suitable size, the incision was extended into the base of the anterior mitral leaflet (Figs 1A, 2). This created a V-shaped defect through the annulus and subvalvular segment of what McAlpine [8] has termed the aortoventricular membrane. The length of the incision, measured from the annulus inferiorly, varied from 5 to 10 mm. Sizing of the orifice was repeated and the appropriate valve was selected. Horizontal mattress sutures of 2-0 Tevdek were passed through the margins of the V (Fig 1B), and the annulus was rimmed with similar sutures. Since the left atrial reflec-

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Preoperative and Postoperative Cardiac Catheterization Data in 8 Patients with Small Aortic Root

Patient's Age (yr) & Sex	Gradient (mm Hg)		Heterograft Valve Size (mm)
	Preop	Postop	
53, F	140	. . .[a]	21
56, F	80	24[b]	23
70, M	78	10	23
64, F	90	7	21
60, F	90	. . .[a]	23
50, F	0[c]	3	23
73, F	0[c]	4	23
71, F	110	15	23

[a] Refused restudy.

[b] Pullback gradient only.

[c] Aortic insufficiency.

tion forms an acute angle at its junction with the anterior mitral leaflet, it was possible to avoid opening this chamber. In the event that the left atrium was entered, it would be closed by simply including the cut edges of the atrium in the same mattress sutures that were used to approximate the opened annulus to the underside of the valve sewing ring.

After the valve was seated and the sutures were tied, a Dacron patch was sutured to the superior margin of the exposed sewing ring, filling the gap created by the annular enlargement (Fig 1C). The ascending aorta was thereby widened as the patch was sutured in place. All air was evacuated from the aorta and the cross-clamp was removed. The heart was defibrillated after 10 to 12 minutes of rewarming.

Results

Aortic cross-clamp time ranged from 46 to 86 minutes in the patients having annular enlargement. This is 12 minutes longer than average clamping time in the overall isolated aortic

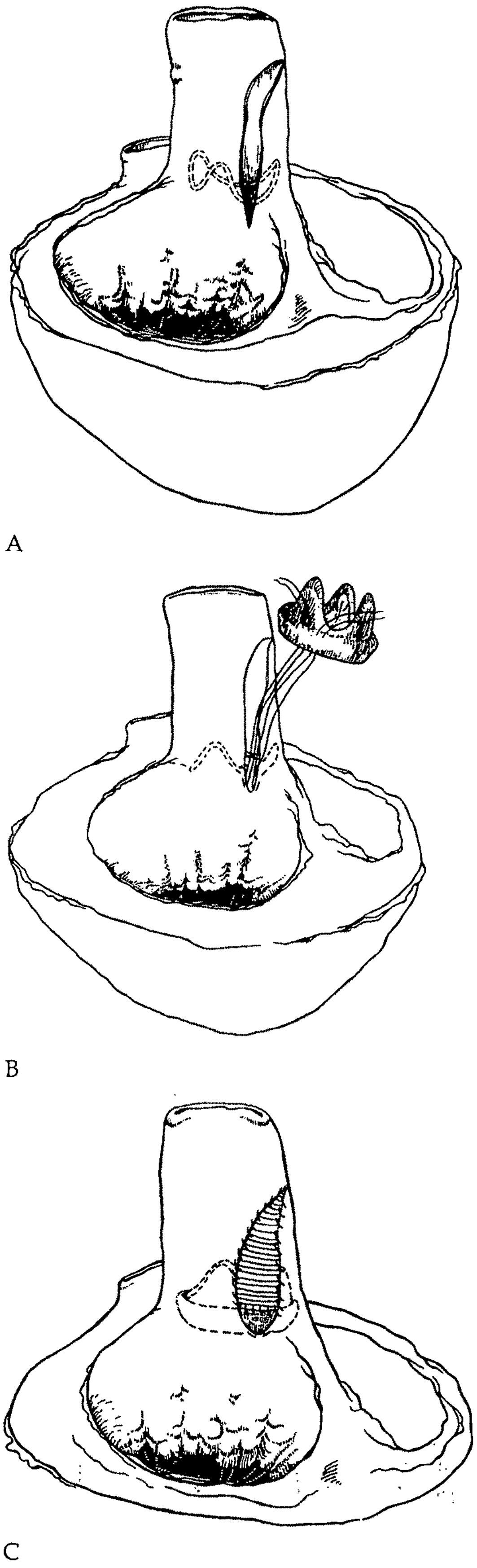


Fig 1. (A) The aortic incision is continued inferiorly in the noncoronary sinus, dividing the annulus and extending into the margin of the anterior mitral leaflet. (B) Placement of horizontal mattress sutures in the defect. (C) The defect is bridged by the sewing ring as the sutures are tied.

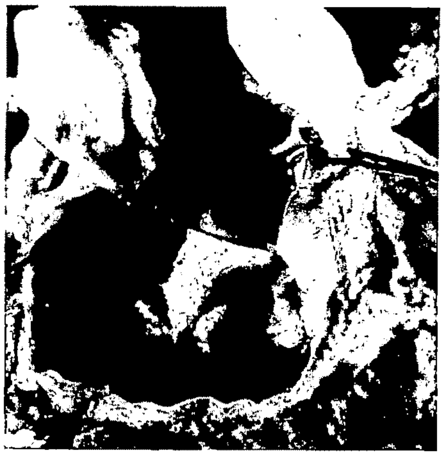


Fig 2. Dissected postmortem specimen with atria removed. Silk sutures placed in the divided aortic annulus show extension of the incision into the margin of the anterior mitral leaflet. (The incision usually ends near the left atrial reflection but has been extended to allow adequate demonstration of the divided aortic annulus.)

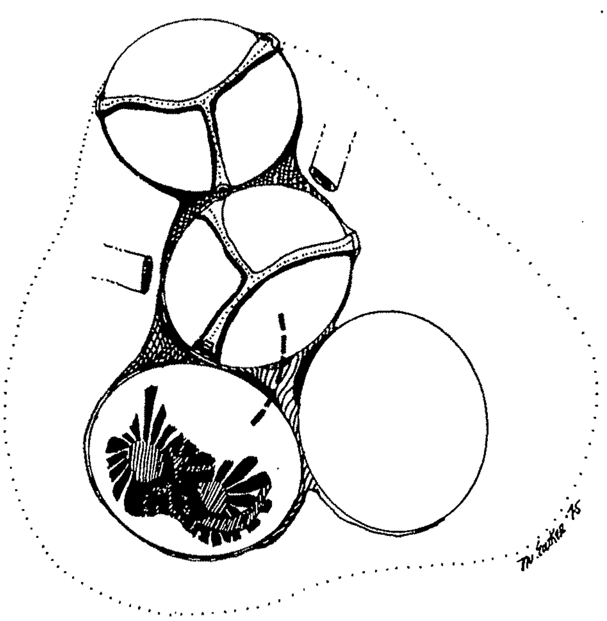
valve replacement group. All 8 patients survived the operation, and 6 of them have had repeat cardiac catheterizations. Ventriculograms in all studied patients showed no alteration in the relationship of the mitral annulus to the aortic outflow tract. One patient had had intermittent bouts of atrioventricular dissociation preoperatively and required insertion of a permanent pacemaker. All patients were alive and remained improved from ten to eighteen months postoperatively.

Comment

All currently available stent-mounted tissue valves have the disadvantage of the orifice being compromised by the mounting device. Björk and his colleagues [2, 3] developed a semicentral-flow, tilting-disc valve because of their dissatisfaction with the high gradients associated with the smaller caged ball valves. The 21 mm Björk-Shiley prosthesis has been used successfully in patients with a narrow aortic root, but it has a resting mean gradient of approximately 20 mm Hg that increases linearly with exercise [3]. Najafi and his co-workers [10] called attention to the difficulty attending valve replacement in patients having a small aorta and described the technique of enlarging the ascending aorta using a Teflon patch. Konno and associates [7] reported a technique for enlarging the aortic annulus by continuing the incision inferiorly to the left of the right coronary ostium into the ventricular septum. This requires opening and enlarging the right ventricular outflow tract as well as repair of the resulting septal defect. Nicks and his associates [11] first described extension of the aortotomy, inferiorly dividing the noncoronary cusp attachment line (annulus) and continuing the incision to the origin of the anterior mitral leaflet. A Dacron patch was sewn to the edges of the defect, thus allowing a larger size (9–10A) Starr-Edwards prosthesis to be used.

Certain anatomical features of the aortic root suggest that the noncoronary sinus is the logical site for expansion of the annulus. Portions of the left and noncoronary sinuses bear a constant relationship to the anterior leaflet of the mitral valve (Fig 3). This portion of the mitral apparatus does not participate in active contraction of the mitral annulus; the remaining three-fourths of the valve, which is contiguous with the ventricular myocardium, does [5]. In addition, the right fibrous trigone is close to the incision line and adds to valve support at this level [6]. The incision passes immediately to the left of the right fibrous trigone, sufficiently pos-

Fig 3. Relationship of the noncoronary and left coronary sinuses to the anterior mitral leaflet. (The incision is represented by the dotted line.)



terior to avoid the conducting system. In our experience, intrusion of a portion of the prosthetic sewing ring in the subvalvular segment of the aortoventricular membrane [8] does not produce mitral valve dysfunction.

Our preference for using the porcine heterograft is supported by the work of Zuhdi's group [13], indicating a low instance of valve failure in patients followed for up to sixty months. Thromboembolic phenomena are negligible, and the valve demonstrates excellent hemodynamics. We prefer to use a porcine heterograft 23 mm or larger, although in those instances when it was necessary to use a smaller valve, the resulting gradient appears to be well tolerated.

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Discussion

DR. HASSAN NAJAFI (Chicago, IL): Dr. Blank has presented an imaginative, bold, and seemingly highly successful contribution to this very difficult area in aortic valve surgery. At the 1975 meeting of the American Heart Association in Anaheim, I was equally impressed with a report from Middlesex, England, that surgeons at that institution had inserted adult-size, fresh aortic homografts in 8 patients 18 months to 15 years of age without any early deaths.

Although Dr. Blank kindly referred to our work in enlarging the aortic root, I have to admit that we have not been courageous enough to extend the incision down or through the aortic valve annulus. But when I received a copy of their fine manuscript, it stimulated me to go to the morgue and test this technique in the autopsy room. I can assure you that it is feasible, although at the end one would wonder whether the junction between the patch, the sewing ring, and the biological tissues, which is really the edge of the left atrium, would withstand the 150 to 200 mm Hg pressure and not bleed. Apparently this has been so in their experience.

Our experience at Presbyterian–St. Luke's Hospital over two and one-half years includes 205 isolated aortic valve replacements. In 48 of these, or one-fourth of the patients, we used Björk-Shiley valves. When I reviewed these cases I noted that the choice of the valve had been governed by the anatomy, mostly narrowing of the aortic root and small size of the valve annulus.

It was interesting that of the 157 patients who received the Starr-Edwards prostheses, a No. 8 valve was used in 11. I think this is a marginal ball-valve prosthesis and should probably not be considered. Certainly a No. 7 should almost never be utilized clinically. The single patient who received a No. 7 valve actually had had a No. 9 Starr-Edwards prosthesis implanted in 1966, and she did well until a year ago when she started having thromboembolic manifestations. At that time the No. 9 valve was removed and a size 7 was inserted. In one year she has gone on to develop cardiomegaly, pulmonary hypertension, and pulmonary congestion, all pointing most probably to a guarded prognosis.

DR. DENTON A. COOLEY (Houston, TX): For relief of some of the more complicated problems involving stenosis of the aortic valve, subvalvular region, and ascending aorta, we have employed a method originally reported by Sarnoff, who used this technique in animals, and by Templeton, who used it in a limited clinical series. The technique creates a double-outlet left ventricle. A woven Dacron graft containing a Hancock porcine valve is sutured to the apex of the left ventricle, and the valve is placed intraabdominally just below the diaphragm. The distal end of the graft is sutured to the proximal abdominal aorta proximal to the origin of the celiac axis.

An angiogram in our first patient, who was operated upon in August, 1975, revealed the unusual appearance of the double-outlet left ventricle and the tortuous course of the conduit into the abdominal aorta. The preoperative left ventricular pressure had been 250 mm Hg systolic, and the gradient across the valve was 100 mm Hg. Postoperatively a residual gradient of 15 mm Hg was present between the ventricle and the ascending aorta.

Since that initial case we have operated on 3 other patients using this technique, a total of 2 girls and 2 male patients with ages ranging from 7 to 36 years. The 36-year-old man had an atypical kind of obstructive cardiomyopathy and had been unsuccessfully operated on twice previously using standard techniques. The gradients in all these patients had exceeded 100 mm Hg preoperatively. Postoperatively the maximum was 20 mm Hg.

It was interesting to quantitate the volume of flow through the ascending aorta against that through the graft conduit using a special flow-tipped catheter. The flows through the conduit were calculated at 29, 41, 33, and 32% of left ventricular output, respectively. In the last 2 patients we temporarily occluded the ascending aorta while the thoracotomy was still open. No changes occurred in systemic arterial pressure, indicating that the entire cardiac output could be delivered through the conduit.

One advantage of this technique may be evident if in the future replacement of the Hancock valve becomes necessary: it could be accomplished rather simply by a laparotomy.

DR. ELLIS L. JONES (Atlanta, GA): Dr. Charles Hatcher and I at Emory University Hospital have used the Hancock aortic prosthesis in approximately 110 patients over the last year and a half with 1 death. We consider the hemodynamics of the valve good.

We have had the opportunity to restudy 22 of these patients with complete right and left heart catheterization at rest and during exercise. The average resting peak systolic left ventricular–aortic pressure gradient for the 19 and 21 mm prostheses was 28 and 25 mm Hg, respectively. By comparison, the average for the 25 mm prosthesis was 20 mm Hg. A similar gradient relationship existed between the smaller and larger prostheses during exercise. It must be noted, however, that most of the individuals in whom the 19 and 21 mm prostheses were used were female patients with a small body surface area and a correspondingly small aortic root. The calculated orifice size showed increasing values, from 0.99 cm^2 for the 19 mm prosthesis to 1.42 cm^2 for the 25 mm prosthesis.

From our experience, we recommend that the largest valves, that is, 23 mm or greater, be considered mandatory for male patients with an average or large body surface area; smaller sizes, such as the 21 mm, still may be used satisfactorily for small women in whom cardiac output is not as great even during exercise. When a slightly larger prosthesis is required, an annulus-enlarging procedure such as described by Dr. Blank may be used. In patients with extreme hypoplasia of the aortic annulus or in young children, a procedure in which the aortic annulus is completely divided midway between the right and left coronary ostia down into the ventricular septum may be used.

DR. CLARENCE S. WELDON (St Louis, MO): Several techniques have been devised for enlarging a small aortic annulus so that the aortic valve may be replaced with a sizable prosthesis. I think these techniques are very helpful. There are, however, some problems they do not solve. One of these is obstruction to left ventricular outflow that cannot be resected. Another is the terrible problem of putting a prosthetic valve in a child; I say terrible problem because I am convinced that we don't have a valve with durability equal to normal life expectancy.

I would like to describe our experience in creating a second left ventricular outflow tract with a valve-bearing conduit interposed between the left ventricular apex and the aorta. A child was operated on at the age of 3 years for biventricular obstruction. He had gradients above 100 mm Hg in both the right and left ventricle. Muscle was resected from the right ventricle, and a myotomy was performed in the left ventricle. The right ventricular pressure gradient was relieved but the left ventricular gradient was not.

We have approached this problem a bit differently from the way Dr. Cooley has. We use a Hancock prosthesis but adapt it by inserting onto the end a rigid cylinder covered with cloth. This cylinder is designed to project into the left ventricular cavity and thus to maintain the opening at the left ventricular apex. Of course, putting a new outflow tract on the other side of the obstruction completely relieves the gradient.

A second patient, a 16-year-old girl, had a very severe midventricular obstruction which at the time of operation appeared to be fibrous tunnel obstruction of the left ventricular outflow tract. She had a gradient of 100 mm Hg in her left ventricle and 50 mm Hg in her right ventricle. We first operated through the aortic valve and removed the subvalvular fibrous tissue. Lower obstruction could not be resected, and therefore we constructed an apical-aortic shunt. We put the distal end of this graft into the infrarenal aorta. I think it works quite well there; it is simple to expose this area, and as Dr. Cooley said, it is also easy to change the valve at some future time when it wears out. This second patient was fairly remarkable. At recatheterization, not only was the gradient absent from her left ventricle, but the gradient of 50 mm Hg due to septal movement had disappeared from her right ventricle. So she now has absolutely no gradients in her heart, and pressures are normal in both sides.

In the first patient, retrograde flow through the apical-aortic outflow tract went all the way to the left subclavian artery. In the second, when the middle of the ventricle was injected, the inferior outflow tract filled only to the level of the diaphragm. The amount of flow through the new outflow tract depends upon the degree of obstruction in the natural outflow tract.

DR. BLANK: I thank the discussants for their comments, particularly Dr. Cooley and Dr. Weldon for describing their interesting management of various small aortic roots.

To answer Dr. Najafi's question, we were fearful that doing an annular enlargement procedure would actually not allow a double-valve replacement. Until late in this study, if we incised the subannular tissues, I always thought we were cutting into the mitral valve. But in a patient who has the V-shaped defect and in whom the annulus has been stretched, if one looks closely at the anatomy, it is apparent that the subannular tissues can be incised from 5 to 10 mm in some instances—achieving, admittedly, a very small increase in transverse diameter.

Another point I would like to make is that the sutures are placed through the subannular tissue and then pulled to the undersurface of the sewing flange on the Hancock prosthesis. The Dacron patch is then sewn to the sewing flange. We consider this a very strong point in the repair. After this study was completed we had a patient in whom the aorta was friable, and we did reinforce it with Teflon-felt pledgets.

Dr. Jones, we were aware of the work you mentioned and have actually communicated with the Emory group. One of the factors that stimulated our interest in this area was the marked increase in cross-sectional area—20 to 25%, depending on the individual valve—when one goes from a 21 to 23 mm porcine heterograft since there is no standardization of orifice diameter in the pig valve at the present time.

I was also aware of the experience from England reported at Anaheim and have written to the surgeon inviting him to come and discuss it with us or to let us know what technique he used. As far as I know, his paper has not been published.

Clinical Evaluation of the Lillehei-Kaster Pivoting-Disc Valve

Peter J. K. Starek, M.D., Lambert P. McLaurin, M.D.,
Benson R. Wilcox, M.D., and Gordon F. Murray, M.D.

ABSTRACT **A four-year clinical evaluation of 133 patients with Lillehei-Kaster pivoting-disc valves has shown that patients with an aortic valve prosthesis have remained free from valve-related problems. Patients with a mitral valve implanted have a satisfactory survival record as calculated by actuarial methods; however, a 10% incidence of valve thrombosis was experienced. Analysis suggests that this may be related to inadequate anticoagulation or use of an inappropriate suturing technique or both.**

The patients enjoyed significant clinical improvement following operation, with no evidence of hemolysis. A history suggestive of postoperative embolization was present in only 1 patient in this series.

The purpose of this paper is to report a four-year clinical evaluation of patients who have undergone valve replacement with the Lillehei-Kaster pivoting-disc valve.

The concept of a pivoting-disc heart valve was introduced by Kaster and Lillehei in 1967 [3]. A clinical version of Kaster's valve first appeared on the market in June, 1970, and since that time has gained wide acceptance, having been utilized by more than 200 cardiac teams in the United States and 300 hospitals in foreign countries. The valve has been implanted in an estimated 25,000 patients to date.* Despite this extensive use, little information has been published on its clinical performance.

Patient Selection and Methods

An unselected series of 133 patients had the Lillehei-Kaster pivoting-disc valve implanted at the University of North Carolina beginning in October, 1971. Preoperatively all patients were in New York Heart Association Functional Class III or IV. Right and left heart catheterization was performed in all individuals. Operation was done utilizing cardiopulmonary bypass with the Bentley† bubble oxygenator and a Sarns‡ pulsatile blood flow pump. Three full-time attending cardiothoracic surgeons were involved in the implantation of all valves in this series, either as primary surgeon or as first assistant. The technique of valve implantation and myocardial preservation varied somewhat among the three surgeons. All patients started receiving anticoagulation with Coumadin§ in the immediate postoperative period. With few exceptions, all patients were maintained on anticoagulants indefinitely.

Postoperatively, patients were followed by periodic visits to the hospital outpatient department. Additional information was obtained by telephone or mail contact with patients and referring physicians. One hundred percent follow-up was thereby achieved in this group of patients.

Results

Five separate groups were identified within the series of 133 patients:

Group 1: simple aortic valve replacement
Group 2: simple mitral valve replacement

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*Telephone conversation January, 1976, with Marshall Kriesel, President, Medical, Inc, 5200 W 78th St, Minneapolis, MN.

†Bentley Temptrol Q-100 Disposable Oxygenator, Bentley Laboratories, Inc, 17502 Armstrong Ave, Irvine, CA 92705.

‡Sarns Model 2000 Pump-Oxygenator System, Sarns, Inc, 6200 Jackson Rd, Ann Arbor, MI 48103.

§Crystalline sodium warfarin, Endo Laboratories, Inc, 1000 Stewart Ave, Garden City, NJ 11530.

Group 3: multiple-valve replacement
Group 4: aortic valve replacement plus other procedures
Group 5: mitral valve replacement plus other procedures

Additional procedures included coronary artery bypass, ventricular aneurysm resection, major valvuloplasty on another valve, or a combination of these, performed at the same time as the valve replacement. The results are summarized in the Table.

Men predominated in the aortic valve replacement as well as the combined replacement groups, whereas women were more numerous when mitral valve replacement was the major procedure. Age varied widely in all groups; however, the average age in Groups 1 and 2 was in the forties. The youngest average age (34 years) was found in Group 3. The average age of Groups 4 and 5 was higher, being 57 and 52 years, respectively.

Early Deaths

The thirty-day operative mortality in Group 1 includes 1 patient who died of an arrhythmia, 1 who died on the operating table with "stone heart," 4 who died of low cardiac output after having sustained intraoperative myocardial infarctions, and 1 who died of renal failure and hyperkalemia.

Three of the 5 early deaths in Group 2 were attributable to technical errors. In 1 patient undergoing operation for a stenotic Kay-Shiley valve, a suture embolus to the left coronary artery resulted in a fatal myocardial infarction. Another patient, who required removal of a malfunctioning Starr-Edwards valve, sustained an injury to the circumflex coronary artery and a resultant myocardial infarction. The third patient died when a suture placed around a valve strut did not allow the disc to open fully. Another patient developed bacterial endocarditis that could not be medically controlled. The infected prosthesis was removed, but the patient remained febrile and died with sepsis and in renal failure. The fifth death in Group 2 was in a patient with a severely decompensated left ventricle and postoperative low-output syndrome resulting in hepatic decompensation, disseminated intravascular coagulation, shock, and death.

In Group 3, 4 of the 5 early deaths were related to low cardiac output associated with gross dilatation of the left ventricle secondary to advanced valvular disease. One patient died of resistant ventricular tachycardia and fibrillation in the early postoperative period. In Groups 4 and 5 the early deaths were all related to the severity of the cardiac disease—either marked left ventricular dysfunction or severe coronary disease manifesting itself in low cardiac output and its associated problems.

Late Deaths

The late mortality in Group 1 (simple aortic valve replacement) consisted of 2 patients; 1 died of renal carcinoma, and the other had a history of chronic arrhythmias that were poorly controlled medically and ultimately led to a fatal arrhythmia. In Group 2 (mitral valve replacement only) 5 of the 9 late deaths were attributable to ar-

Results of Valve Replacement with the Lillehei-Kaster Pivoting-Disc Valve

					Mortality				Postop NYHA Class			
Group	Procedure	No. of Patients	Sex (M/F)	Age (yr)	Op	Late	Emboli	Thrombosis	I	II	III	IV
1	Simple AVR	45	27/18	22–70 ($\overline{47}$)	7	2	0	0	19	15	2	
2	Simple MVR	48	15/33	13–66 ($\overline{42}$)	5	9	1	4	16	13	5	
3	Multiple valve	15	9/6	14–62 ($\overline{34}$)	5	2	0	1 (mitral)	3	4	1	
4	AVR + other	16	12/4	17–73 ($\overline{57}$)	9	0	0	0	3	4		
5	MVR + other	9	4/5	24–58 ($\overline{52}$)	3	2	0	1		4		
Total		133	67/66	13–73 ($\overline{46}$)	29	15	1	6	41	40	8	

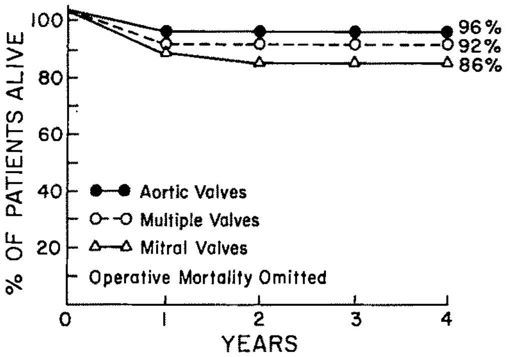
AVR = aortic valve replacement; MVR = mitral valve replacement.

rhythmias. These individuals died suddenly after having otherwise done quite well. At postmortem examination no emboli or valve problems were found. One of the 9 patients died of a cerebral hemorrhage associated with improper anticoagulation therapy; 2 others died of thrombosed mitral valves. An intraabdominal catastrophe, very likely an embolus to the mesenteric artery, caused the death of 1 individual, the only patient in the series with a probable embolus. In Group 3 (multiple-valve replacement) 1 patient died of an arrhythmia; no abnormalities of the valve were demonstrated postmortem. Progressive congestive heart failure due to a grossly decompensated left ventricle without evidence of valve malfunction led to the other death in the group. There have been no late deaths in Group 4 (aortic valve replacement plus other procedures). In Group 5 (mitral valve replacement plus other procedures) 1 patient died of a thrombosed mitral valve. The other death was in a patient with subacute bacterial endocarditis and severe tricuspid regurgitation who required reoperation four months postoperatively. The patient did not survive the second procedure.

In patients surviving operation, actuarial curves show a four-year survival of 95.7% for patients with simple aortic valve replacement, 86% for patients with mitral valve replacement, and 92% for patients with multiple-valve replacement [1] (Fig 1).

Analyzing all patients who were late survivors with an aortic valve in place shows that 55 individuals were followed for 1,329 months, an average of 24 months per patient, with no incidence of embolization or thrombosis. Fifty-nine late survivors with a mitral valve in place were followed for 1,258 months, an average of 21 months per patient. In this group there has been 1 fatal embolus and 6 instances of mitral valve thrombosis. Of these 6 patients, 3 died without reoperation and 3 were saved by emergency operation.

Fig 1. Actuarial curves comparing survival of patients with Lillehei-Kaster aortic valves, mitral valves, and multiple valves.



Hemolysis secondary to heart valve replacement was not evident in any of the groups, nor were there problems directly related to mechanical failure of valves. Eight of the 89 surviving patients are in Functional Class III. The remaining 81 patients are evenly distributed between Classes I and II.

Comment

Many new prosthetic heart valve designs have been introduced on the market over a period of years. In making a decision to utilize a new heart valve, the surgeon needs information regarding the hemodynamic performance of the valve as well as its clinical performance in terms of freedom from valve-related complications such as embolism, thrombosis, and mechanical failure. As has been recently reported from this institution [4], the Lillehei-Kaster pivoting-disc valve possesses superior hemodynamic properties. Since long-term clinical performance does not necessarily coincide with excellent hemodynamic qualities, however, close scrutiny of the patients' clinical course over a number of years is required. The four-year follow-up presented in this paper reveals that patients with a Lillehei-Kaster aortic valve are free from mechanical problems, embolization, hemolysis, and thrombosis. On the other hand, patients with a mitral valve prosthesis have a less satisfactory record.

A 10% incidence of mitral valve thrombosis demands a closer look at the problem. Maintenance of careful anticoagulation is quite difficult for many patients from remote rural areas. It seems likely that inadequate anticoagulation was a contributing factor in at least 4 of the valve thromboses, and possibly in all 6. The anticoagulation status is unknown in 1 of the 6 patients with a thrombosed valve. Four of the patients had inadequate anticoagulation with

Coumadin, documented shortly before valve thrombosis, and 1 patient was known to have difficulty in following instructions regarding her Coumadin dosage. In 5 of the 6 patients, valve thrombosis progressed rapidly over a period of a few days to either reoperation or death. In retrospect, only 1 patient developed gradually increasing symptoms of thrombosis over a period of months.

In 4 of the 5 patients with rapidly progressing thrombosis, the valves had been sewn in with horizontal mattress sutures reinforced by Teflon pledgets placed on the ventricular side of the annulus [2]. With this technique, malfunction of the Lillehei-Kaster valve may be induced by forcing the tissue annulus close to the struts and disc. To analyze this problem suturing techniques were studied in the laboratory. Figure 2A demonstrates the proximity of the annulus and valve struts when pledgets are placed on the ventricular side of the annulus. Conversely, this tissue crowding is less apt to occur when pledgets are placed on the atrial side of the annulus (Fig 2B).

Five of the 6 mitral valve thromboses occurred within the first few months after implantation. In 1 patient the valve was found to be stenotic after a year's time. At reoperation tissue ingrowth was seen on the ventricular side without the frank thrombosis found in the other 5 valves. Personal communication in January, 1976, with several other surgeons* utilizing this valve did not reveal the high incidence of mitral valve thrombosis found in our group of patients.

Our overall experience with Lillehei-Kaster valves is good. All patients who were in Functional Class III or IV preoperatively improved one or two classes following their operation, reflecting the favorable hemodynamic performance of these valves. This four-year follow-up of 133 patients with Lillehei-Kaster pivoting-disc valves shows that the prosthesis performed extremely well in the aortic position. There, the valve has been virtually problem free, and we consider it the prosthesis of choice in the aortic position. In the mitral position, the 10% incidence of valve thrombosis may be the result of inadequate anticoagulation or use of an inappropriate suturing technique or both. The late survival, as calculated by actuarial methods, is quite acceptable.

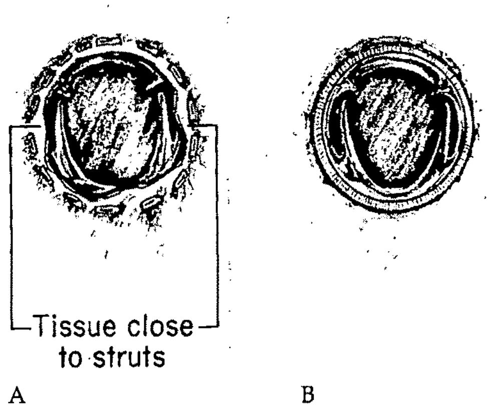


Fig 2. Comparison of suturing techniques, ventricular view. (A) Annulus and valve struts are in proximity when pledgets are placed on the ventricular side of the annulus. (B) Pledgets placed on the atrial side of the annulus.

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Discussion

DR. JOHN C. COLES (London, Ont, Canada): I enjoyed Dr. Starek's paper very much. It is highly commendable and very important that major complications be reported. Our own experience with this valve in the mitral position has been dissimilar; perhaps this is related to time.

At the University of Western Ontario Victoria Hospital, we have had experience with 175 Lillehei-Kaster valves in 159 patients ranging in age from 20 to 83 years. Our early practice was to use the valve only in high-risk patients, for those over 70 years of age, for infectious endocarditis, for emergency valve replacement, and to replace ball valves. The initial results were so rewarding that we now use this valve routinely.

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The durability of the Lillehei-Kaster valve, the immediate postoperative cardiac output, and the red blood cell and platelet survival have impressed us. At comparable valve sizes, the gradients are significantly less than for ball valves. Hemolysis is not a problem in the absence of perivalvular leak.

It is very important to remove sufficient subvalvular tissue when using this valve in the mitral position, and also to avoid too large a prosthesis.

We have had occasion to reoperate on 2 patients who had a Lillehei-Kaster valve in the mitral position. In 1 the disc was impeded from full opening by subvalvular tissue, and we resected the prosthesis and replaced it with a Lillehei-Kaster valve of the same size. The second patient had a No. 28 valve, which was too large. The disc was not opening completely, and it was replaced with a No. 25 prosthesis.

I would like to ask Dr. Starek if he thinks this may be one of the reasons for the high incidence of thrombus in the mitral prostheses in his series.

DR. DEMETRE M. NICOLOFF (Minneapolis, MN): We have used the Lillehei-Kaster valve since January, 1972, and have placed 364 valves since that time, 269 of them done by myself or my colleague, Dr. William Lindsay. Our operative mortality for aortic valve replacement is 7.7% with a late mortality of 5.8% over the four-year period. For mitral valve replacement it is 5.6 and 2.8%, respectively. Late deaths were not caused by thrombosis of the valve. In all cases, the cause of death was not related to the prosthesis.

Twenty-three patients had double-valve replacement (aortic and mitral). The operative mortality was 13% with a late mortality of 13% over the four-year period. Again, we had no prosthesis-related late mortality.

As far as late morbidity with aortic valve replacement, we had 1 instance of embolism, which was transient; it occurred three weeks postoperatively and the symptoms lasted about two hours. There has been no malfunction of the valve in the aortic position. We have had 3 perivalvular leaks, none requiring reoperation.

With mitral replacement we have had 4 embolic episodes, a 4% incidence. Two of these were transient neurological findings, while the other 2 resulted in very firm hemiparesis. There were 3 perivalvular leaks and 3 prosthesis malfunctions. The latter might be a misnomer—it was not the prosthesis that malfunctioned; I think it was the surgeon, who put too large a prosthesis into the mitral annulus. Two of these patients have been reoperated upon, and it was obvious that the prosthesis had been placed into an annulus that was small for the size of the valve and that the ventricular muscle and endocardium had prevented the disc from functioning properly.

Postoperative catheterization was done in 43 patients with a Lillehei-Kaster prosthesis in the aortic position at six months to one year following operation. The data show that 10 patients with No. 14 valves have a mean peak systolic gradient of 46 mm Hg (range, 28 to 70) with a functional valve area of 0.8 cm^2. All patients who had had the No. 14 valve inserted were women with severe calcific stenosis. There was no operative mortality in this group, and all are now in Class 1 functional status. With valve sizes 16 to 25 the mean peak systolic gradients were 25 to 6 mm Hg, respectively. Functional valve areas for these prostheses were 1.1 to 2.1 cm^2.

DR. FREDERICK B. PARKER, JR. (Syracuse, NY): We have utilized this valve since 1973 in 144 patients, 72 of whom had mitral valve replacement; 63, aortic valve replacement; and 9, double-valve replacement. Total follow-up has been 1,677 patient-months. Six patients have had peripheral emboli, for an incidence of 4.1%. Four were from the mitral position and 2 from the aortic. Four patients had had anticoagulation and 2 had not. None have had residual defects. Unless there is some contraindication, we routinely give anticoagulants to all patients having valve replacement.

We have seen 6 late deaths. Two of these were from continued congestive heart failure following valve replacement, 2 from arrhythmias, 1 from valve dysfunction, and 1 was unrelated to the valve replacement. Postmortem examinations were obtained in 4 of the 6 patients. In 1 of the 2 who died from arrhythmia there was clot in the atrium but not on the valve itself. The patient who died of valve dysfunction had clot within the valve that had obstructed valve function. Both of these patients had received anticoagulants. They represent the only disquieting episodes that we have had with this valve.

I agree with Dr. Starek that his high incidence of thrombosis probably represents a technical error from placing pledgets on the ventricle side. In about two-thirds of our mitral valve replacements we have utilized pledgets, but they have been placed on the atrial side.

To date we are very pleased with this valve, particularly in the aortic position. We are still using it in the mitral position but have some reservations about it. Close follow-up is imperative if this prosthesis is to be fully evaluated.

DR. RICHARD A. DE WALL (Dayton, Ohio): I have used the Lillehei-Kaster valve in all positions since August of 1971 in 126 patients. This includes 72 patients who received mitral prostheses for whom the observation period is now 122 patient-years. My only bad experiences were due to placing too large a prosthesis in the mitral annulus. This occurred in 3 patients, in whom the prosthesis slowly thrombosed over the course of a few months. All were successfully reoperated upon with replacement by a smaller prosthesis. The prosthesis should be sized to fit easily within the annulus, but not on top of it.

Only 1 of these patients had a transient neurological episode, with full recovery. We gave anticoagulants to all mitral valve recipients with the exception of an 8-year-old boy who has been maintained for two years on aspirin therapy alone with no problems.

The Lillehei-Kaster prosthesis has also served my patients well in the aortic position. This experience constitutes 54 patients, representing 83 patient-years of use. No complications have been encountered. About two-thirds of these patients have received anticoagulant therapy and one-third have not.

We have seen no perivalvular leaks or hemolytic problems.

DR. ARTHUR C. BEALL (Houston, TX): I think it is particularly important to reemphasize the necessity of presenting our difficulties with prosthetic valves. However, I also think this needs to be put into context with the patient's disease. We have a benefit/risk ratio to consider, and this is particularly important to keep in mind as we meet in Washington in this day of consumer protection and imminent medical device legislation. Despite occasional prosthetic valve complications, most of the patients are improved considerably. However, these complications again demonstrate the necessity for very careful and permanent follow-up. If there is a change in symptoms or in heart sounds, the patient should be restudied, and with many thrombosed valves or other types of problems the patient can be reoperated on successfully.

As an example, among more than 18,000 of the Teflon version of our valves, 29 instances of disc variance have been reported. A large number of these patients have been reoperated on successfully. Many of the deaths could have been avoided if someone had thought to restudy the patients.

I reported to you in the past the problem of broken struts with our mitral prosthesis in the original Model 105 configuration with Pyrolite. With the change to the Model 106, which has now been in use for more than two years, there is yet to be a broken strut. I think the problem has been corrected.

This paper from Chapel Hill was interesting in regard to the thrombosed valves presented, because one of the supposed advantages of the tilting-disc valve is lower gradients. You cannot completely cover a tilting-disc valve with cloth because the disc descends into the orifice. We accepted that the central-occluder valves probably would have higher gradients, but we could cover their orifices with fabric and therefore decrease the incidence of thromboembolism. However, in the January, 1976, issue of *The Journal of Thoracic and Cardiovascular Surgery*, the group from Chapel Hill has reported gradients across the Lillehei-Kaster prosthesis that are similar to those seen with central-occluder valves.

DR. JOHN C. CALLAGHAN (Edmonton, Alta, Canada): I would like to present our experience and to support Dr. Starek's conceptual thoughts at the end of his paper.

Dr. Fisk, before he emigrated from Canada down to the warmer climate of Phoenix, reviewed our studies of the patients in whom we had used the Lillehei-Kaster valve. We too were sensitive to the fact that although a great number of these valves were being put in, there seemed to be very few clinical reports.

In this study, during the period March, 1973, to March, 1975, we inserted 150 consecutive Lillehei-Kaster valves. Fifty of these fitted into Dr. Starek's mitral prosthesis group. And suffice it to say, our patients were similar to his with 1 exception: a patient who had no kidneys to start with and none afterward and who died on dialysis about seven months later. There was an average follow-up of one year.

We used the same type of suture technique that Dr. Starek described, placing pledgets on the upper (or atrial) side of the annulus. During this study, the finding we were most impressed with was that when we reviewed this series by personal contact with our patients, we did not find a single instance of embolization.

We had no surgical deaths, and of the 3 patients who died late, 1 was an Eskimo from the far Arctic who had had no anticoagulation. When he came in we thought there would be thrombus in the valve, but we could find no evidence of it. And there was 1 other patient, with multivalvular disease, who was not treated adequately.

We at the University Hospital, Edmonton, are impressed that this appears to be an extremely safe valve. I have had experience with aliquots of almost every other valve developed over the last few years, and I have been impressed that this one causes fewer problems, produces no embolization, and is the most trouble-free valve that I have had the pleasure of putting in.

DR. C. WALTON LILLEHEI (St Paul, MN): The pivoting-disc prosthesis has been implanted in more than 25,000 patients during the past five and one-half years. This large experience makes possible some significant observations concerning its comparative freedom from the usual valve-related complications.

First is its functional durability. To date, there has not been a single instance of early or late mechanical failure of the valve. This notable record is unique in the history of prosthetic valve replacement. And as you have heard here today from others, the hemodynamic performance has been excellent, the incidence of embolism has been very low, and there has been a uniform absence of hemolysis.

However, one caveat is in order. It is possible to misuse this valve in the mitral area by selecting a prosthesis that is too large for the size of the left ventricle. It is not the size of the annulus or of the left atrium that is important in sizing the mitral prosthesis. Fortunately, there is a considerable margin of safety, but if the prosthesis is grossly oversized in relation to the left ventricle, then it is possible for one of the struts to become imbedded, to a variable degree, in the adjacent mural myocardium and to provoke scar tissue growth that may gradually impede disc motion over a period of some weeks to months.

This problem occurred twice early in our series, and at reoperation the cause of the late onset of "restenosis" was manifest. Since those observations, restraint has been exercised in choice of the size of the mitral prosthesis, correlating it with the size of the left ventricle. No such caution is necessary in the aortic area, where the largest possible prosthesis to fit into the subcoronary area is recommended.

Dr. Starek kindly provided me with a copy of his paper, and I have compared the sizes of mitral prostheses used by his group with those used by my associates and me. His group used a preponderance of the larger sizes, with 56% of all patients receiving the largest size (25 mm) compared with only 13% in our series. Likewise, they utilized the three smaller sizes in only 17% of their patients, whereas we have used those same sizes in 57.5%.

Due to the considerable safety margin, even this use of substantially larger sizes would not likely have created the frequent late flow problems had it not been for the unusual prosthesis suturing technique described. This method, which narrowed the upper portion of the left ventricle, was utilized in approximately one-third of the Chapel Hill patients. It is significant, as Dr. Starek has emphasized, that 4 of the 6 patients with valve thrombosis came from the minority whose valves were sutured by this method. It is noteworthy that despite this problem, embolism remained low.

The final point I wish to make in this regard is the fact that the excellent hemodynamics of this prosthesis make it unnecessary to strive to insert the very largest prosthesis possible into the mitral area. From the postoperative recatheterization data presented here by Dr. Nicoloff, and earlier by Dr. Starek (J Thorac Cardiovasc Surg 71:123, 1976), it may be noted that the low diastolic gradients and large functional cross-sectional areas of the pivoting-disc prostheses in the mitral position do not significantly change when the largest (25 mm) and the medium prostheses (22 or 20 mm) are compared.

It is difficult to be specific in a clinical matter such as this, but generally, in a woman of small or average stature with a normal-sized left ventricle, we would tend to use a size 18 to 20 prosthesis. In a man of average stature with a normal-sized left ventricle, as seen in mitral stenosis, I would tend to use the 20 to 22 mm sizes, reserving the 25 mm valve only for patients with an enlarged left ventricle.

Thus, with these relatively minor safeguards, I believe that patient experience with this prosthesis will continue to be a very happy one, as confirmed by the impressive number of favorable reports from others here today.

DR. STAREK: I thank the discussants for their comments. All mentioned the problems created by insertion of a valve too large for a particular tissue annulus. I doubt that improper choice of prosthesis size was a cause of our problems, since the thrombosed valves did not appear early in our series. Five of the valve thromboses occurred in the third year of our experience. Three of the 6 surgeons implanting valves were senior residents. The attending surgeons acted as first assistants for every operation that they did not personally do, so the residents were carefully supervised.

The only thing we could temporally correlate with the valve thromboses was the introduction of a new suturing technique. I feel certain that this was the major cause of the valve thrombosis in our series.

We have recently reported our hemodynamic evaluation of the Lillehei-Kaster prosthesis and consider it, from that viewpoint, a very superior valve.

Major Pulmonary Resection for Bronchogenic Carcinoma in the Elderly

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ABSTRACT **The results of major pulmonary resection in 58 patients greater than 70 years of age were reviewed. The histological distribution and extent of nodal metastases in this age group are the same as in younger patients. The absolute five-year survival rate for the 55 patients undergoing curative resection was 30% (17 patients). It was 36% (11 patients) for those patients with squamous cell carcinoma and 22% (5 patients) for those with adenocarcinoma. The operative mortality was only 14% (8 patients). Of the 49 patients treated by lobectomy, 17 lived five years or more free of disease, whereas none of the 6 patients treated by pneumonectomy survived five years.**

The five-year survival rate of 30% in this series of elderly patients treated by major pulmonary resection makes resections in such patients with bronchogenic carcinoma worthwhile.

As the number of individuals entering the elderly age brackets continues to rise, so does the incidence of bronchogenic carcinoma. In Belcher's series of patients operated upon between 1950 and 1955, the largest proportion were in their fifties [2]. In his most recent series many patients were in their late sixties, with 40% between ages 65 and 74 [3]. A similar trend has been reported by others [1, 8, 10]. Since many persons over 70 with bronchogenic carcinoma have marginal cardiovascular status or pulmonary reserve, physicians are often reluctant to consider them for pulmonary resection. Nevertheless, operative intervention continues to be the only effective therapy for this otherwise lethal disease.

Limited pulmonary resection has been advocated by Jensik and associates [10] for elderly individuals who have bronchogenic carcinoma and a marginal cardiopulmonary reserve. Although such operations preserve pulmonary tissue, they are applicable only to those lesions which are peripheral in location and not greater than 3 to 5 cm in diameter. A dilemma exists for those patients with lesions that cannot be removed with a lesser procedure, as one must weigh the risk of operation against the benefits of resection.

Since 1959, 58 patients greater than 70 years of age have undergone major curative pulmonary resection (lobectomy or pneumonectomy) for bronchogenic carcinoma at the University of Michigan Medical Center. An additional 17 patients were diagnosed as having bronchogenic carcinoma but did not undergo resection, although it was technically possible, because of severe cardiopulmonary insufficiency. The purpose of this report is to review our experience with the operative treatment of bronchogenic carcinoma in patients over 70 years of age to determine the benefits, if any, of such therapy and to see if an unduly high risk is involved in pulmonary resection.

Clinical Experience

During the ten-year period from 1959 to 1969, 75 patients greater than 70 years of age were diagnosed as having bronchogenic carcinoma. Based on standard chest roentgenograms, laminagrams, and bronchoscopy, all these patients were judged to be suitable candidates for pulmonary resection. Seventeen patients were denied operation because of either poor general condition or cardiopulmonary reserve insufficient to enable them to tolerate the proposed pulmonary resection. The remaining 58 patients underwent pulmonary resection. In none of these was there radiographic evidence of mediastinal or subcarinal lymph node involvement.

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Whether lobectomy or pneumonectomy was carried out depended upon the location of the lesion and the extent of the carcinoma. Lobectomy was carried out whenever technically feasible. Pneumonectomy was performed for lesions that could not be removed with a lesser procedure. The perihilar and hilar lymph nodes were removed en bloc with the primary lesion whenever possible. Following resection the superior mediastinal, subcarinal, subaortic, and paraesophageal lymph nodes were completely removed. We considered the operation to be curative if all the gross tumor was excised. Three patients did not receive curative resections, 2 because of the proximal extent of their tumor and 1 because of pulmonary reserve insufficient for him to tolerate the resection necessary for complete tumor removal. Only those 55 patients undergoing curative resection are included in this analysis.

Group I (Nonoperative)

Twelve patients with squamous cell carcinoma, 4 with adenocarcinoma, and 1 with undifferentiated carcinoma did not undergo resection because of poor general condition or insufficient cardiopulmonary reserve. The tumors were centrally located in 10 patients and in the more peripheral regions of the lung in the remaining 7 patients. There was no difference between this group of patients and the operated group with respect to age, size of tumor, or histological classification of the tumor.

All 17 patients received radiation therapy, and none lived five years. The average survival time of those undergoing irradiation was 7.7 months. Sixteen of these patients died from either carcinomatoses or local recurrence, and 1 patient died from myocardial infarction 6 months after radiation therapy.

Group II (Operative)

The age and sex distribution of the patients is listed in Table 1. The ratio of male to female patients was approximately 10:1. The absolute five-year survival rate for the 55 patients undergoing curative resection was 30% (17 patients). The histological distribution, extent of lymph node metastases, and survival rate are listed in Tables 2 and 3. Thirty-five patients had neither hilar nor mediastinal metastases. Thirteen of them were alive and free from disease at the end of five years. Peribronchial or hilar metastases were found in only 9 patients, and 2 of these patients survived five years free of disease. Mediastinal metastases were found in an additional 11 patients, 2 of whom received radiation therapy in the immediate postoperative period and were five-year survivors.

Of the 49 patients treated by lobectomy, 17 lived five years or more, a five-year survival rate of 34%. On the other hand, none of the 6 patients treated by pneumonectomy survived five years free of disease.

Table 1. Age and Sex Distribution of 55 Elderly Patients Operated Upon for Bronchogenic Carcinoma

	Age & No. of Patients		
Sex	70–75	76–79	80
Male	39	6	5
Female	4	1	0

Table 2. Five-Year Survival According to Metastases and Cell Type Among 55 Elderly Patients Operated Upon for Bronchogenic Carcinoma

	All Cell Types		Squamous Cell Carcinoma		Adenocarcinoma	
Metastases	No. Treated	Survivors	No. Treated	Survivors	No. Treated	Survivors
None	35	13	18	7	15	5
Hilar only	9	2	5	2	4	0
Mediastinal (with radiation therapy)	11	2	7	2	3	0

Table 3. Bronchogenic Carcinoma, 1959–1970, in 55 Elderly Patients: Overall Five-Year Survival According to Histological Cell Type

Cell Type	No. of Patients Treated	Five-Year Survivors
Squamous cell	30	11
Adenocarcinoma	22	5
Large cell undifferentiated	2	0
Oat cell carcinoma	1	1

Table 4. Bronchogenic Carcinoma, 1959–1970, in 55 Elderly Patients: Causes of Late Death

Cause of Death	No. of Patients
Unknown	7
Carcinomatosis or local recurrence	25
Causes other than carcinoma	10

In 35 patients the cause of death was known (Table 4). Most of the patients who did not live five years died of malignant disease. The results in this group of patients are classified according to age and are listed in Table 5.

The majority of patients who had resection died within two years of operation, either from recurrence of their carcinoma or from arteriosclerotic cardiovascular disease. However, of those patients who survived the first two years, the majority lived for a reasonably long time and the quality of survival has been considered satisfactory.

Postoperative Mortality

The overall mortality rate for those undergoing resection was 14%. One of the 6 patients undergoing pneumonectomy and 7 of the 49 having lobectomy died. The causes of early postoperative death are listed in Table 6.

Comment

The factors that influence long-term survival following pulmonary resection for bronchogenic carcinoma remain a subject of debate. It is generally agreed that there is no difference among survivors with reference to the size of the primary lesion, its degree of differentiation, the extent of resection, and the presence or absence of blood vessel invasion. There is a difference of opinion, however, regarding the prognostic significance of age. Higgins and Beebe [9] stated that the length of survival is strongly influenced by, among other things, the age of the patient. In their review these authors found that the prognosis becomes successively poorer with increasing age. On the other hand, Connelly and associates [7] observed little correlation between age and survival when adjustments were made for normal life expectancies. Slack and coworkers [16] found that, except for operative deaths, age had little relationship to survival in a surgical series. Similar conclusions were reached by Veronesi [18]. Series reported by Bignall and Moon [4], Cleland [6], and Van Nostrand and associates [17] found no particular correlation between age and survival.

The results of our study are similar to those of Connelly [7], Slack [16], and Sensenig [15] and their colleagues: age per se does not have an adverse influence on long-term survival following pulmonary resection for bronchogenic car-

Table 5. Five-Year Survival According to Age Among 55 Elderly Patients Operated Upon for Bronchogenic Carcinoma

	Overall		Squamous Cell Carcinoma		Adenocarcinoma	
Age	No. Treated	Survivors	No. Treated	Survivors	No. Treated	Survivors
70–75	43	13	24	8	17	4
76–79	7	2	3	2	3	0
80	5	2	3	0	2	1

Table 6. Bronchogenic Carcinoma, 1959–1970; Causes of Early Postoperative Deaths Among 55 Elderly Patients

Cause of Death	No. of Patients
Respiratory insufficiency	4
Cerebrovascular accident	1
Myocardial infarction	2
Pulmonary embolus	1

cinoma. The 30% five-year survival in patients greater than 70 years who had pulmonary resection for bronchogenic carcinoma compares favorably with the five-year survival of 36%, reported from our own and several other institutions [11, 12], in previously treated patients under 70 years old who had pulmonary resection for bronchogenic carcinoma.

A similar survival rate of 30% was reported by Evans [8] in a series of 81 patients above 70 years of age who underwent either lobectomy or pneumonectomy as treatment for their bronchogenic carcinoma. The reasons for the low cure rate following pneumonectomy in our series cannot be determined since the number of patients is too small. It may be related to the extent of disease rather than to the extent of resection, because all 6 of these patients had either hilar or mediastinal metastases.

On the basis of these and other studies, the decision whether or not to perform a major pulmonary resection in patients greater than 70 years old should be based not upon the patient's age but rather upon his cardiovascular status and pulmonary reserve. Retrospectively, 2 of 8 patients in our series who died following pulmonary resection should have been refused operation. Evans reported a similar postoperative mortality of 20% in patients greater than 70 years undergoing major pulmonary resection for bronchogenic carcinoma. If one eliminates from consideration those patients who should not have been operated upon, it is interesting to note that this series of geriatric patients had a mortality rate of 11%, which compares favorably with mortality figures of these and other studies derived without regard to age.

The critical question that remains to be answered is what constitutes inadequate cardiovascular or pulmonary reserve for a proposed pulmonary resection. This is a subject of continuing controversy, and it is extremely difficult to obtain uniform information about it from the literature. On the basis of our clinical experience as well as the studies of Boushy [5], Reichel [14], Olsen [13], Van Nostrand [17], and their coworkers, the following guidelines have been used to indicate insufficient pulmonary reserve for a proposed pulmonary resection:

1. Resting hypercapnia ($P_{CO_2} > 45$ mm Hg) or hypercapnia with exercise.
2. Hypoxemia ($P_{O_2} < 50$ mm Hg) at rest or following exercise despite hyperventilation.
3. An $FEV_1 < 2{,}000$ cc, $FVC < 2{,}000$ cc, or MVV $< 50\%$ of predicted values in those in whom a pneumonectomy is required.
4. An $FEV_1 < 1{,}500$ cc in those in whom a lobectomy is required.
5. A calculated $FEV_1 < 800$ cc as determined preoperatively by combining spirometry with a ventilation-perfusion scan.

From a cardiovascular point of view, the presence of overt congestive heart failure, unstable angina, or a recent myocardial infarction (less than 6 months previously) should be considered an indication of inoperability.

Patients with peripheral lesions no greater than 3 to 5 cm in diameter with cardiopulmonary reserve insufficient for a lobectomy may tolerate a lesser operation such as wedge resection or segmentectomy. These procedures should be applied because, in our own experience and in that of others, no patient with unresected carcinoma of the lung has survived five years following the diagnosis.

Although the number of patients in our series is too small to be of statistical significance, the five-year survival of 30% in those patients undergoing major pulmonary resection for bronchogenic carcinoma has encouraged us to continue this program in elderly patients afflicted with this disease.

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The Superior Approach for Correction of the Supracardiac Type of Total Anomalous Pulmonary Venous Return

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ABSTRACT **An alternative approach for correction of supracardiac (type I) total anomalous pulmonary venous return is described. A median sternotomy is used. The posterior wall of the left atrium and the common pulmonary venous trunk are exposed through the transverse sinus. A direct anastomosis between these structures, ligation of the systemic-venous connection (vertical vein), and closure of the interatrial septal defect results in a one-stage repair. In our experience with the supracardiac anomaly in 20 patients, we have found that this approach consistently affords better exposure than other techniques currently in use for surgical correction of this anomaly.**

Current surgical therapy has greatly altered the unfavorable natural course of total anomalous pulmonary venous return (TAPVR) [1, 6–8, 18]. Since surgical correction of the supracardiac type of TAPVR was reported in 1951 [10], several approaches have been described to improve access to the common pulmonary venous trunk and to redirect the pulmonary venous return to the left atrium [3–5, 10–12, 14, 15, 17].

In the supracardiac (type I) variation of this anomaly, one of us observed that excellent exposure of the common pulmonary venous trunk and superoposterior aspect of the left atrium could be obtained through the transverse sinus. The proximity of these structures and their accessibility through the transverse sinus facilitate creation of the largest possible anastomosis between the left atrium and the common pulmonary venous trunk. We now have used this technique in 20 patients with type I TAPVR and have been uniformly impressed with the exposure and the ease with which the anastomosis can be carried out [16].

The superior approach through the transverse sinus is our approach of choice for operations on the mitral valve and for the removal of left atrial myxoma [9, 13].

Technique

A median sternotomy incision is used, avoiding either pleural space. Both the superior and inferior venae cavae and the femoral artery or ascending aorta are cannulated in the routine manner. The persistent vertical vein is identified from within the pericardial sac and is surrounded with a tie but not occluded. The common pulmonary venous trunk is identified as it courses parallel to the superoposterior aspect of the left atrium, subjacent and parallel to the right main pulmonary artery. It is mobilized from its position posterior to the pericardium. Cardiopulmonary bypass is instituted, and core cooling to 28°C is accomplished. This allows reduction of the total-body perfusion rate if bronchial blood flow is excessive. Topical hypothermia using 4°C Ringer's lactate cools the heart further and protects the myocardium during the period of aortic cross-clamping.

The aorta is retracted to the left, and mobilization of the roof of the left atrium and the common pulmonary venous trunk is completed. Dependency caused by the superior vena caval cannula helps to expose the common vein and left atrium on the right side, thus completing the necessary exposure (Fig 1). Two tapes are passed around the common pulmonary venous trunk; during creation of the anastomosis these serve to elevate and intermittently occlude the common pulmonary venous trunk (see Fig 2). The tie about the persistent vertical vein is pulled up to occlude it. Parallel incisions are made in the left atrium and along the common pulmonary ve-

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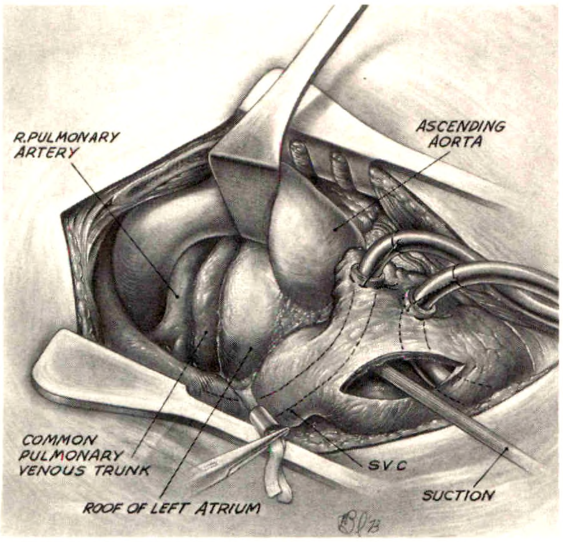

Fig 1. Surgical exposure, showing left atrium and common pulmonary venous trunk as seen in the transverse sinus. (SVC = *superior vena cava.)*

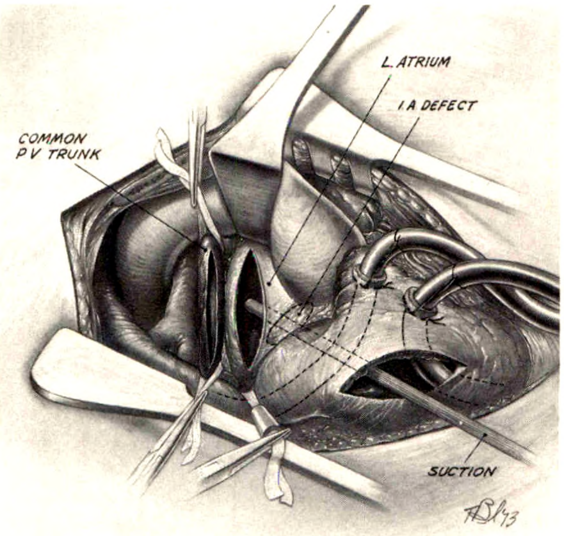

Fig 2. A suction cannula passed through the atrial septal defect (IA defect) *into the left atrium helps keep the field free from blood during the anastomosis.* (PV trunk = *pulmonary venous trunk;* IA defect = *interatrial defect.)*

nous trunk. A suction cannula passed through a right atriotomy and through the atrial septal defect into the left atrium keeps the field free of any blood (Fig 2).

As large an anastomosis as possible is then fashioned between the two structures, using a continuous suture of 6-0 nonabsorbable material (Fig 3). Keeping the leftward tape around the

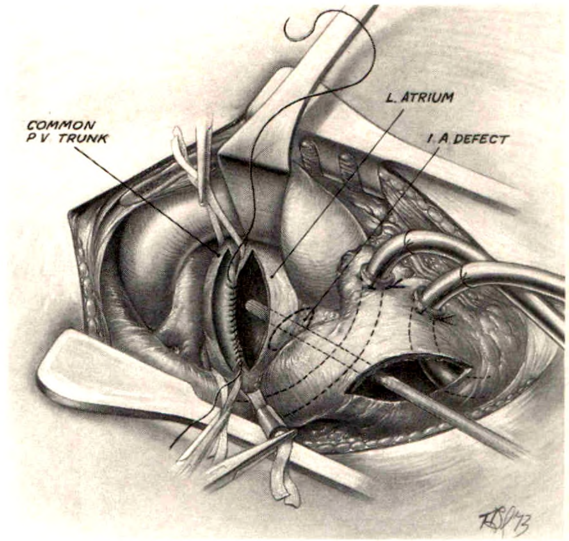

Fig 3. Tapes placed around the common pulmonary venous trunk (common PV trunk) *serve to elevate and temporarily occlude it during the anastomosis.* (IA defect = *interatrial defect.)*

pulmonary venous trunk pulled up and releasing the tie about the persistent vertical vein prevents overdistention of the pulmonary venous circuit during the anastomosis. Following completion of the anastomosis, the vertical vein is tied off. The atrial septal defect is closed in the usual manner through the right atrium. The routine precautions are taken to prevent air-trapping on the left side of the heart.

Comment

Muller [10] in 1951 reported successful partial correction of TAPVR by anastomosing the left atrial appendage to the common venous trunk through a left thoracotomy. Five years later, in 1956, Burroughs and Kirklin [2], using extracorporeal circulation, corrected TAPVR in a patient by creating a side-to-side anastomosis between the common venous trunk and the left atrium and closing the atrial septal defect. In 1957, Cooley and Ochsner [4] described a patient operated upon through a bilateral anterior thoracotomy in whom the anastomosis between the common pulmonary venous trunk and left atrium was performed through the right atrium. Cooley and Collins [3] later presented their experience with 10 patients using this approach. Shumacker and King [15] described a modification of Cooley's technique, performing the anastomosis almost entirely by working outside the heart from the right side. This technique, they believed, facilitates creation of an anastomosis of maximal size. In 1958 Senning [14] operated upon a patient through a right-sided thoracotomy, anastomosed the left atrial appendage to the common pulmonary venous trunk, and closed the atrial septal defect. In the same year, Ehrenhaft and his associates [5] reported a successful operation in a 10-year-old boy.

Mustard and co-workers [11] in 1962 advocated a left anterolateral thoracotomy, dividing the sternum but not entering the right pleural space. A side-to-side anastomosis between the left atrium and common pulmonary venous trunk was carried out, and the persistent vertical vein or atrial septal defect was left open. They advocated a staged operation for the supracardiac type of anomalous pulmonary venous return. In 1964 Williams and colleagues [17] reported a median sternotomy approach. In the 4 patients they operated upon, the anastomosis between the common pulmonary venous trunk and left atrium was performed from behind by lifting the heart and holding the apex upward. In 1970 Roe [12] described his experience using a left posterolateral approach through the fourth intercostal space.

Currently there is no unanimity concerning the surgical approach for correction of the supracardiac type of anomalous pulmonary venous return. Though many surgeons prefer a median sternotomy for this operation, others believe that a transthoracic approach has certain advantages. The inherent benefits of a median sternotomy are the avoidance of either pleural space, the facility of achieving cardiopulmonary bypass, and the standardization of approaches for surgically correctable cardiac lesions. A thoracotomy approach, on the other hand, violates the pleural space, compresses the lung, and makes cannulation of the cavae difficult.

Several methods of approaching the posterior left atrial wall and common pulmonary venous trunk have been described. Creation of a large communication between the anomalous pulmonary venous trunk and left atrium is desirable. The operation described by Williams and associates [17] is ideal for repair of the infradiaphragmatic type of TAPVR; this approach is awkward, however, in the supracardiac variety. When the anastomosis is completed and the heart is returned to its normal position, it is difficult to be sure that the anastomosis will lie correctly. Kinking of the pulmonary veins, if not the anastomosis itself, is possible. Shumacker's technique [15] has the advantage of not requiring dislocation of the heart. However, the atria must be retracted leftward and the limits of the left atrium defined from the right. Posteriorly the pericardial attachments must also be divided, then the heart must by necessity be compressed. Construction of the leftward portion of the anastomosis can be carried out readily, while the rightward or final portion of the suture line is cumbersome. Vision from the assistant's side is limited.

From our experience, using the superior approach through the transverse sinus always affords excellent exposure of the common pulmonary venous trunk and the left atrium. The area is readily accessible through a median sternotomy, a minimal amount of retraction is necessary, and the heart is not compressed or displaced. All parts of the anastomosis are readily visible, and the exposure offers the surgeon and his assistant an excellent view of the repair.

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Intraoperative Placement of Central Venous Pressure Monitoring Cannulas

Francisco Gosalbez, M.D., Donald J. Magilligan, Jr., M.D.,
and Julio C. Davila, M.D.

ABSTRACT **A method for placement of central venous pressure monitoring and fluid administration catheters is described which we have found quite useful in our practice for the past three years in patients undergoing sternotomy incisions, most commonly for cardiac procedures.**

One or more large-bore intravenous cannulas are essential in the management of patients requiring prolonged or rapid administration of blood and fluids and continuous monitoring of central venous pressure [1]. We have found the technique presented here, and previously used by the services of the National Heart Hospital in London,* to be quite useful.

After the sternum is split in the midline, anterior mediastinal structures are dissected, dividing the thymus. The innominate vein is exposed over a 3 to 4 cm segment. A small pursestring suture is placed on the anterior surface of the vein using 5-0 synthetic suture material. Through a small stab wound above the clavicle, a Teflon catheter† with needle stylette (16- to 18-gauge) is advanced underneath the sternum and directed toward the pursestring (Figure, A). The anterior wall of the vein is pierced with the needle, which is then withdrawn, and the catheter is advanced to a satisfactory position (Figure, B). The pursestring is then tied. A holding suture is placed in the skin and tied to the cannula. It is convenient to hold the anterior surface of the vein with a thumb forceps while the needle is being introduced to avoid perforating the posterior wall. The position of the catheter can be digitally controlled in the superior vena cava once the pericardium is opened. At the time of sternum closure the position of the catheters should be checked to ensure that they are not caught between the two halves.

In more than 50% of our patients we have placed two catheters through the same pursestring in the vein wall (see Figure, B). Withdrawal is accomplished by cutting the holding suture in the skin and pulling the catheter out 24 hours to 15 days after operation. The two catheters can be removed simultaneously or one at a time on different occasions. We have not seen important bleeding from the vein needle hole on removal or mediastinal widening on subsequent roentgenograms.

This technique has been used routinely since 1972 in about 200 procedures every year, including infants (in whom 20-gauge catheters are used) and patients with cyanotic congenital heart disease. The posterior wall of the superior vena cava was perforated by the catheter at its entrance into the right atrium in 1 patient because the vena cava snare tightened around both the cardiopulmonary bypass cannula and the catheter; since then we have avoided advancing the catheter very far into the superior vena cava. In 1 other patient, reexplored for bleeding several hours postoperatively, one of the catheters was found dislodged and lying in the anterior mediastinum. Blood being administered through this catheter was coming out through the chest tubes (no other bleeding points were found). It is easy to check the position of the catheter periodically by aspirating blood from it.

The only situation in which this technique has been found troublesome is in second or third operations in patients who have had previous midsternotomy incisions, in whom dissection to expose the innominate vein may be tedious.

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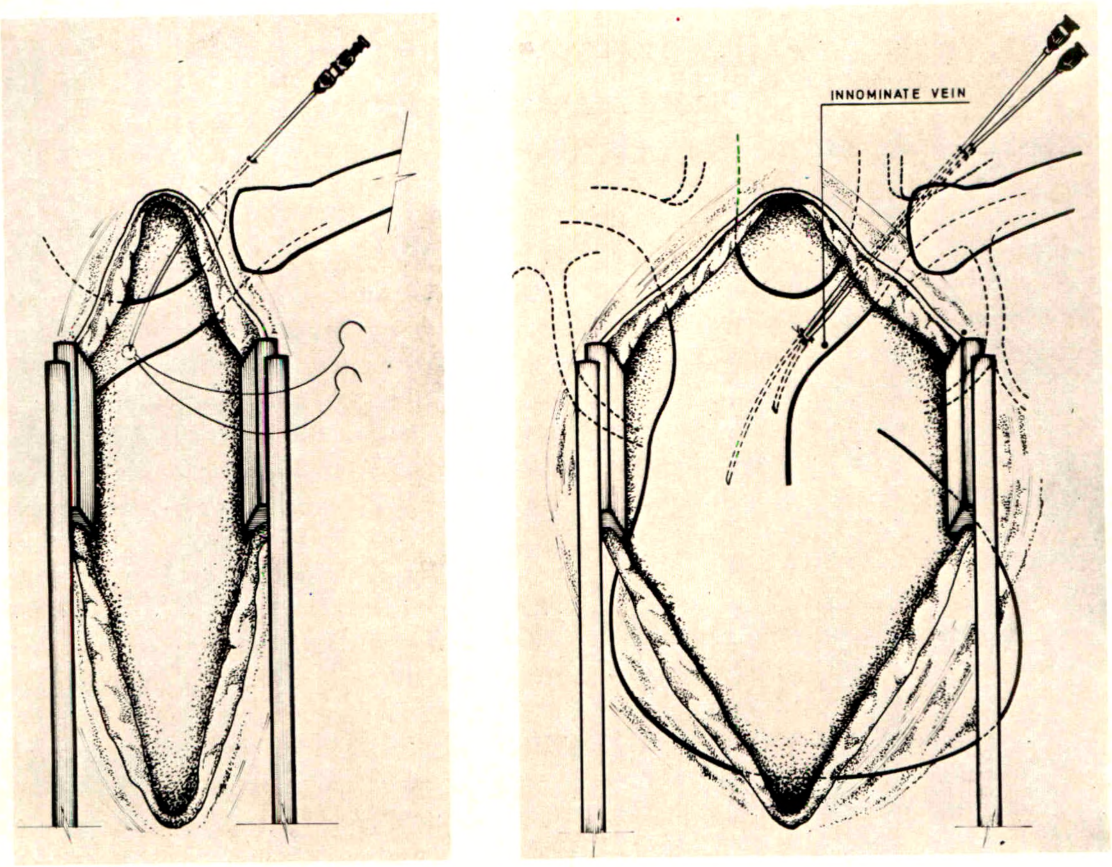
*Gonzalez-Lavin L: Personal communication, 1972.

†Model 6734 BD Longdwel Catheter, Becton-Dickinson Co, Rutherford, NJ.



A

B

(A) A pursestring suture has been placed on the anterior wall of the innominate vein, and the needle is being advanced. (B) Two cannulas are in position.

CASE REPORTS

Left Ventricular Wall Rupture after Mitral Valve Replacement: Report of Successful Repair in 2 Patients

Seong Chi, M.D., Richard Beshore, D.O., and Lorenzo Gonzalez-Lavin, M.D.

ABSTRACT **Left ventricular wall rupture after mitral valve replacement, though uncommon, is a disastrous complication when it does occur. We have experienced this problem in 2 separate instances. Successful treatment was accomplished by suturing a large prosthetic patch over the entire area of laceration and hematoma.**

Mitral valve replacement can now be carried out with low operative mortality and good long-term results [1–3]. Problems inherent in the surgical procedure remain, however, the most drastic of which is left ventricular wall rupture. In a recent review Zacharias and co-workers [4] found a 100% mortality in 6 patients with this complication among 1,154 operations for mitral valve replacement in one institution and 13 deaths among 19 cases reported in the literature.

We have experienced this disastrous complication twice. In both instances successful treatment was accomplished by suturing a large prosthetic patch over the entire area of laceration and hematoma. The case histories and surgical technique employed are described.

Patient 1

A 54-year-old white woman with a long history of rheumatic heart disease and increasing disability due to mitral regurgitation was admitted to Ingham Medical Center for elective mitral valve replacement. She was found to be in Functional Class III by New York Heart Association criteria. Operation was performed on April 23, 1974.

Following right anterolateral thoracotomy, cardiopulmonary bypass was instituted with high flow and moderate systemic hypothermia to 28°C. Utilizing myocardial perfusion and electrical fibrillation, the diseased mitral valve was easily replaced with a large Beall valve inserted with interrupted sutures of 2-0 Tevdek. Excessive bleeding was apparent when bypass was terminated, and complete cardiopulmonary bypass was reinstituted.

Inspection of the external surface of the left ventricle revealed a laceration in the posterior wall. To achieve better exposure, the sternum was transected, the aorta was cross-clamped, and a left ventricular sump was placed at the apex. Massive bleeding was found to originate from a laceration 4 cm in length involving the entire thickness of the left ventricular wall. This tear was located very close to the atrioventricular groove, near the left circumflex coronary artery, and was surrounded by hematoma (Fig 1). Several attempts to suture the laceration were unsuccessful. A large Dacron patch was placed over the entire area of laceration and hematoma and sutured to healthy myocardium with multiple interrupted sutures of 4-0 Prolene, taking care to avoid the left circumflex coronary artery (Fig 2). After the aorta was unclamped, the heart vented, and the ventricular sump removed, the heart began to contract forcefully. Cardiopulmonary bypass was discontinued once hemostasis was secured, and the heart maintained adequate output. Postoperative chest drainage was 1,500 ml per 24 hours (83 ml per square meter of body surface area) for the first postoperative day and subsequently tapered off.

The patient's course was complicated by a short episode of tubular renal failure that was managed successfully by the usual medical means. She was discharged on May 11, 1974. When last seen in the cardiac follow-up clinic two years after operation she was asymptomatic, and the prosthetic valve was functioning well.

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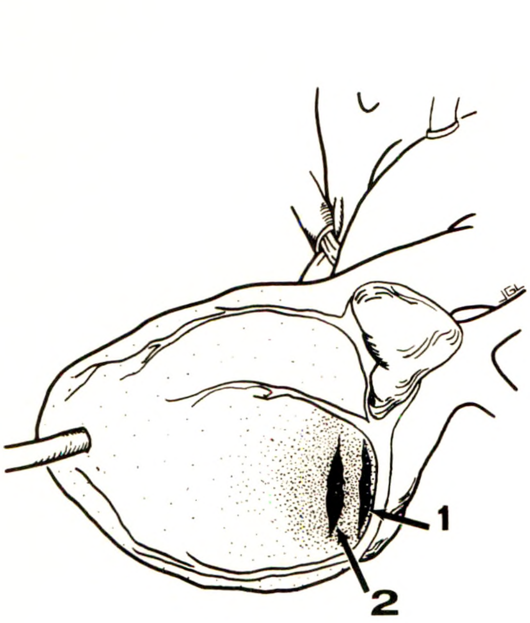


Fig 1. The sites of laceration in the 2 patients are indicated by their respective patient number.

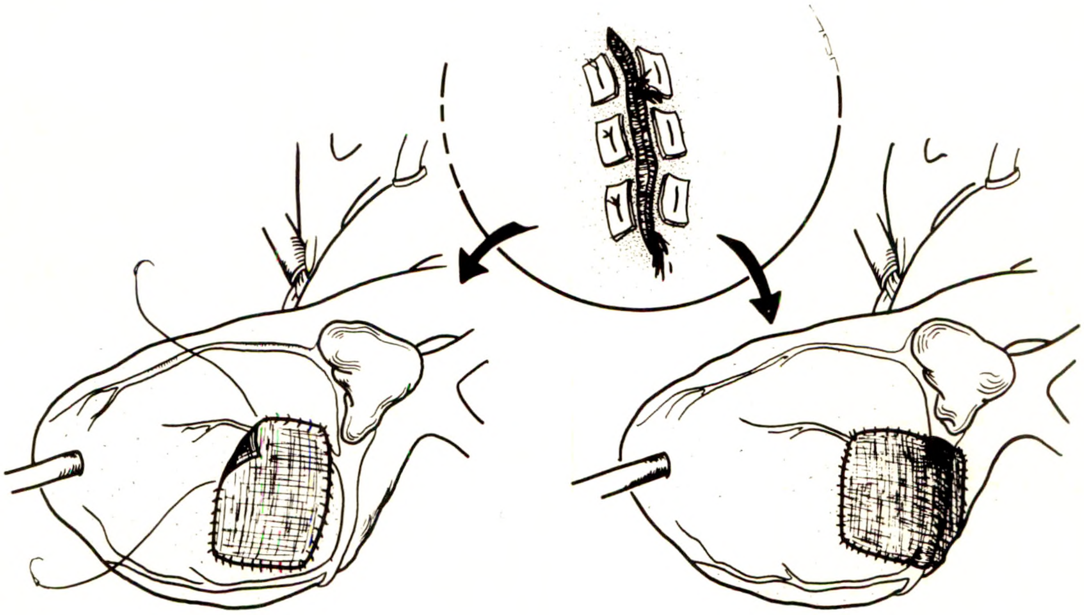
Patient 2

A 62-year-old white woman with a long history of rheumatic heart disease and severe mitral stenosis was admitted to Ingham Medical Center for elective valve replacement. She was found to be in Functional Class IV, and an operation was performed on July 25, 1974.

Through a midline sternal-splitting incision, cardiopulmonary bypass was instituted with high flow and moderate systemic hypothermia to 28°C. The diseased mitral valve was replaced with a 33 mm Hancock porcine xenograft valve* inserted with multiple interrupted sutures of 2-0 Tevdek during 30 minutes of anoxic arrest. She was able to sustain good cardiac output at the conclusion of bypass. After decannulation, however, profuse bleeding was encountered coming from the posterior surface of the heart. Following urgent recannulation and return to cardiopulmonary bypass, the aorta was cross-clamped and a sump was placed in the apex of the left ventricle.

On inspection of the posterior wall of the left ventricle, a laceration 4 cm in length was found 1 cm below the atrioventricular groove and surrounded by a large hematoma (see Fig 1). When the heart was retracted to the right, the sewing ring of the xenograft valve protruded slightly

Fig 2. The first step in the repair consisted of placing multiple interrupted mattress sutures reinforced with Teflon felt pledgets. Due to persistent bleeding, a large, two-way-stretch Dacron graft was then sutured to healthy myocardial tissue at a distance from the laceration with a running suture.



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*Hancock Laboratories, Anaheim, CA.

through the laceration. A strip of Teflon felt was placed on each side of the laceration and incorporated into multiple interrupted mattress sutures in an attempt to control the excessive hemorrhage. Due to continuing bleeding, a large, two-way-stretch Dacron patch was then fashioned so as to cover the entire area of laceration and hematoma; it was sutured to healthy myocardium with a running stitch of 3-0 Prolene (see Fig 2). Hemostasis was readily obtained, and after cardiopulmonary bypass was discontinued the heart was able to cope with the circulatory load. Inotropic drugs were given for the first 48 hours. Chest drainage postoperatively was 675 ml per 24 hours (42 ml per square meter).

The patient's postoperative course was complicated by transient tubular renal failure and postperfusion psychosis. Mechanical ventilation was required for five days. She was discharged from the hospital on August 26. When last seen in the cardiac follow-up clinic twenty months after the operation, she was asymptomatic and the xenograft valve was functioning well.

Comment

The apparent mechanism of posterior left ventricular wall rupture following mitral valve replacement has been clearly outlined by Zacharias and associates [4]. Traction on the mitral valve leaflets and papillary muscles during their excision may invaginate some of the left ventricular wall at the base of the papillary muscles. Blood infiltrating this denuded and weak area produces a large hematoma that dissects the entire thickness of the myocardium and perforates the ventricle when forceful ventricular contractions are resumed.

The valve prosthesis itself appears to have no direct bearing in this complication, although in some instances the prosthesis may be seen protruding through the laceration when the heart is retracted to visualize the posterior wall of the left ventricle.

Control of bleeding by direct suture of the perforation is obviously unsuccessful due to surrounding hematoma with friable myocardium. Interrupted sutures between two Dacron strips also fail because bleeding into and between individual muscle bundles reduces their holding strength. Stitches taken wide enough to be effective would compromise potentially friable myocardium and, in some cases, deprive a major portion of the heart of its blood supply. The patch technique involves tailoring a Dacron patch large enough to cover the entire affected area so that it can be sutured to good holding tissue. A patch that is large relative to the lesion must be used. The size factor probably distributes the pressure beneath the patch over a greater area, reducing the tension on individual sutures and thus the possibility of suture tearing. The patch itself provides a firm backing for clot formation.

This technique has been used with success in 2 patients. We attribute the favorable outcome to early diagnosis and prompt treatment as well as to the use of a large Dacron patch.

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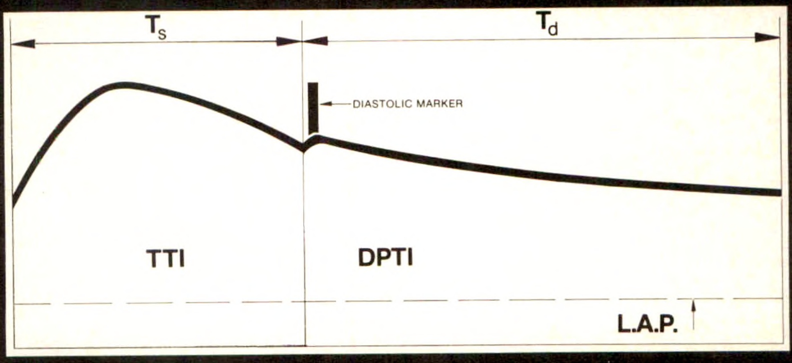

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*Philips, P.A., Marty, A.T., and Miyamoto, A.M.: A Clinical Method For Detecting Subendocardial Ischemia After Cardiopulmonary Bypass, J. THORAC, CARDIOVASC. SURG

The open chest. Another opening for staph*?

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Valve replacement: a procedure that can at once sustain life *and* predispose to infection. Although identification of the infectious organism may be difficult, a delay in treatment could result in invasion of the endocardium. The implicated organism may be a penicillinase-producing staph. Progression can be swift and devastating.

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Appropriate specimens for bacteriologic studies to determine the causative organisms and their susceptibility to nafcillin should be taken prior to the first dose of antibiotic.† And, if those studies subsequently implicate organisms other than penicillinase-producing staphylococci sensitive to nafcillin, discontinue it and administer the appropriate antibiotic.

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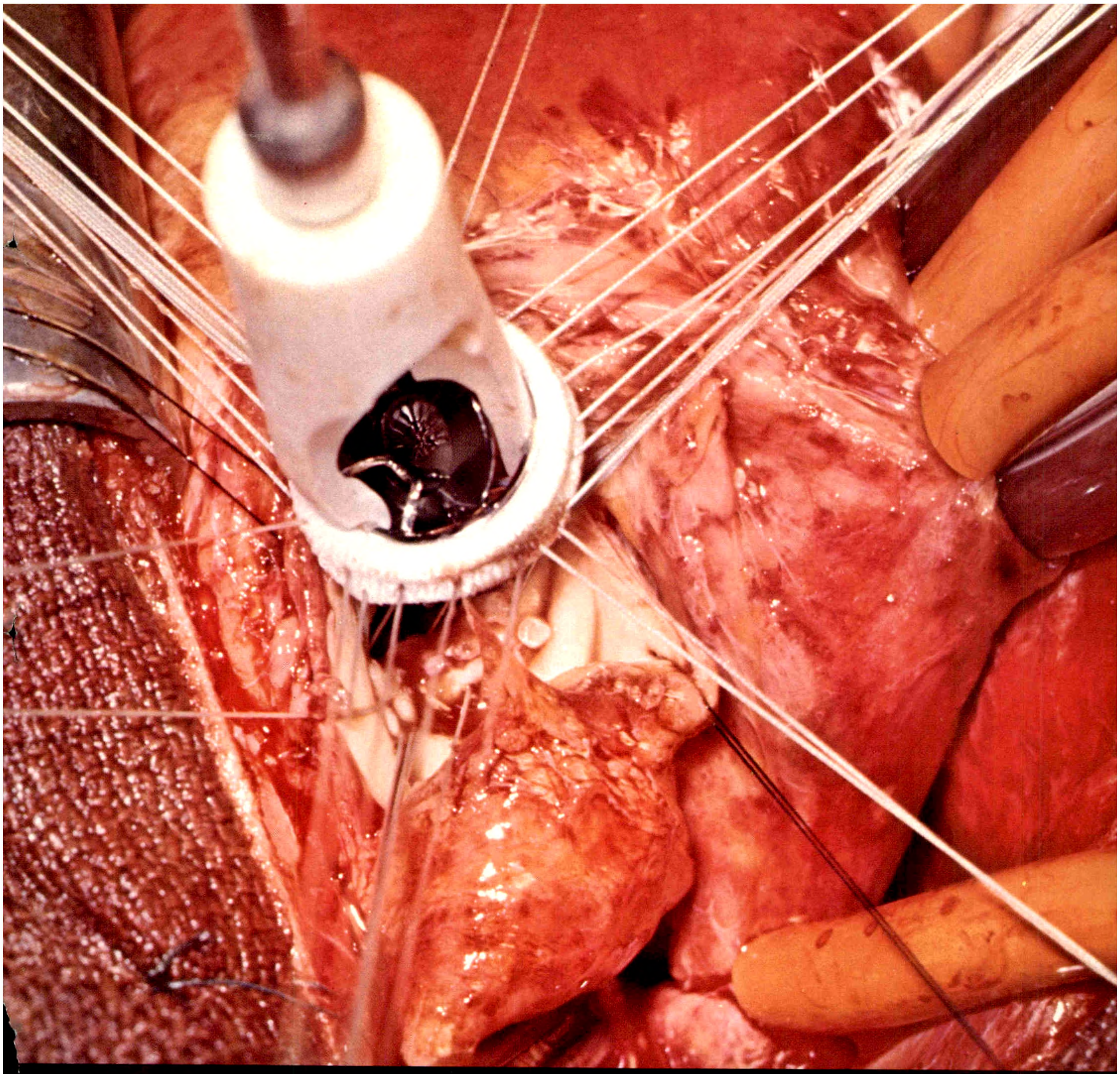

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Disc Susceptibility Tests: Quantitative methods that require measurement of zone diameters give the most precise estimates of antibiotic susceptibility. One such procedure* has been recommended for use with discs for testing susceptibility to penicillinase-resistant penicillin-class antibiotics. Interpretations correlate diameters on the disc test with MIC values for penicillinase-resistant penicillins. With this procedure, a report from the laboratory of "susceptible" indicates that the infecting organism is likely to respond to therapy. A report of "resistant" indicates that the infecting organism is not likely to respond to therapy. A report of "intermediate susceptibility" suggests that the organism would be susceptible if high dosage is used, or if the infection is confined to tissues and fluids (e.g., urine) in which high antibiotic levels are attained.

*Bauer, A.W., Kirby, W.M.M., Sherris, J.C., and Turck, M.: Antibiotic Testing by a Standardized Single-Discs Method, Am. J. Clin. Pathol., 45:493, 1966; Standardized Disc Susceptibility Test, FEDERAL REGISTER 37:20527-29, 1972.

Indications: Although the principal indication for nafcillin sodium is in the treatment of infections due to penicillinase-producing staphylococci, it may be used to initiate therapy in such patients in whom a staphylococcal infection is suspected. (See Important Note below.)

Bacteriologic studies to determine the causative organisms and their sensitivity to nafcillin sodium should be performed.

In serious, life-threatening infections, oral preparations of the penicillinase-resistant penicillins should not be relied on for initial therapy.

Important Note: When it is judged necessary that treatment be initiated before definitive culture and sensitivity results are known, the choice of nafcillin sodium should take into consideration the fact that it has been shown to be effective only in the treatment of infections caused by pneumococci, Group A beta-hemolytic streptococci and penicillin G-resistant and penicillin G-sensitive staphylococci. If the bacteriology report later indicates the infection is due to an organism other than a penicillin G-resistant staphylococcus sensitive to nafcillin sodium, the physician is advised to continue therapy with a drug other than nafcillin sodium or any other penicillinase-resistant semi-synthetic penicillin.

Recent studies have reported that the percentage of staphylococcal isolates resistant to penicillin G outside the hospital is increasing, approximating the high percentage of resistant staphylococcal isolates found in the hospital. For this reason, it is recommended that a penicillinase-resistant penicillin be used as initial therapy for any suspected staphylococcal infection until culture and sensitivity results are known.

Methicillin is a compound that acts through a mechanism similar to that of nafcillin sodium against penicillin G-resistant staphylococci. Strains of staphylococci resistant to methicillin have existed in nature and it is known that the number of these strains reported has been increasing. Such strains of staphylococci have been capable of producing serious disease, in some instances resulting in fatality. Because of this there is concern that widespread use of the penicillinase-resistant penicillins may result in the appearance of an increasing number of staphylococcal strains which are resistant to these penicillins.

Methicillin-resistant strains are almost always resistant to all other penicillinase-resistant penicillins (cross resistance with cephalosporin derivatives also occurs frequently). Resistance to any penicillinase-resistant penicillin should be interpreted as evidence of clinical resistance to all, in spite of the fact that minor variations in **in vitro** sensitivity may be encountered when more than one penicillinase-resistant penicillin is tested against the same strain of staphylococcus.

Contraindications: A history of allergic reaction to any of the penicillins is a contraindication.

Warnings: Serious and occasionally fatal hypersensitivity (anaphylactoid) reactions have been reported in patients on penicillin therapy. Although anaphylaxis is more frequent following parenteral therapy it has occurred in patients on oral penicillins. These reactions are more apt to occur in individuals with a history of sensitivity to multiple allergens.

There have been reports of individuals with a history of penicillin hypersensitivity reactions who have experienced severe hypersensitivity reactions when treated with a cephalosporin. Before therapy with a penicillin, careful inquiry should be made concerning previous hypersensitivity reactions to penicillins, cephalosporins, and other allergens. If an allergic reaction occurs, appropriate therapy should be instituted, and discontinuation of nafcillin therapy considered. The usual agents (antihistamines, pressor amines, corticosteroids) should be readily available.

Precautions: As with any potent drug, periodic assessment of organ system function, including renal, hepatic and hematopoietic, should be made during prolonged therapy.

The possibility of bacterial and fungal overgrowth should be kept in mind during long-term therapy. If overgrowth of resistant organisms occurs, appropriate measures should be taken.

The oral route of administration should not be relied upon in patients with severe illness, or with nausea, vomiting, gastric dilatation, cardiospasm or intestinal hypermotility.

Safety for use in pregnancy has not been established.

Particular care should be taken with intravenous administration because of the possibility of thrombophlebitis.

Adverse Reactions: Reactions to nafcillin sodium have been infrequent and mild in nature. As with other penicillins, the possibility of an anaphylactic reaction or serum sickness-like reactions should be considered. A careful history should be taken. Patients with histories of hay fever, asthma, urticaria, or previous sensitivity to penicillin are more likely to react adversely.

The few reactions associated with the intramuscular use of nafcillin sodium have been skin rash, pruritus, and possible drug fever. As with other penicillins, reactions from oral use of the drug have included nausea, vomiting, diarrhea, urticaria, and pruritus.

Parenteral Administration: It is recommended that parenteral therapy be used initially in severe infections. The patient should be placed on oral therapy with this product as soon as the clinical condition warrants. Very severe infections may require very high doses.

Intravenous Route: The required amount of drug should be diluted in 15 to 30 ml. of Sterile Water for Injection, U.S.P., or Sodium Chloride Injection, U.S.P., and injected over a 5- to 10-minute period. This may be accomplished through the tubing of an intravenous infusion if desirable.

Stability studies on nafcillin sodium at concentrations of 2 mg/ml and 30 mg/ml in the following intravenous solutions indicate the drug will lose less than 10% activity at room temperature (70° F.) during the time period stipulated:

Isotonic sodium chloride	24 hours
5% dextrose in water	24 hours
5% dextrose in 0.4% sodium chloride solution	24 hours
Ringer's solution	24 hours
M/6 sodium lactate solution (conc. of 30 mg/ml)	24 hours

Discard any unused portions of intravenous solutions after 24 hours.

Only those solutions listed above should be used for the intravenous infusion of Unipen® (nafcillin sodium). The concentration of the antibiotic should fall within the range of 2 to 30 mg/ml. The drug concentrate and the rate and volume of the infusion should be adjusted so that the total dose of nafcillin is administered before the drug loses its stability in the solution in use.

There is no clinical experience available on the use of this agent in neonates or infants for this route of administration.

This route of administration should be used for relatively short-term therapy (24-48 hours) because of the occasional occurrence of thrombophlebitis, particularly in elderly patients.

Intramuscular Route: The clear solution should be administered by deep intragluteal injection immediately after reconstitution. After reconstitution, keep refrigerated (2°-8° C.) and use within 7 days or keep at room temperature (25° C.) and use within 3 days.

Oral Administration: Beta-hemolytic streptococcal infections should be treated for at least 10 days to prevent development of acute rheumatic fever or glomerulonephritis.

If oral therapy is inadequate, resort to parenteral nafcillin sodium.

After mixing, the oral solution must be stored in a refrigerator. Discard any unused portion after one week.

Supplied: INJECTION (VIALS)—Supplied in vial sizes of 500 mg., 1 gram, and 2 gram nafcillin sodium as the monohydrate, buffered. When reconstituted as recommended, the contents of each vial provides, respectively, 2-, 4- or 8-ml. of nafcillin sodium solution equivalent *per ml.* to 250 mg. nafcillin buffered with 10 mg. sodium citrate. Film-coated TABLETS—containing nafcillin sodium as the monohydrate, equivalent to 500 mg. nafcillin buffered with calcium carbonate. CAPSULES—containing nafcillin sodium, as the monohydrate, equivalent to 250 mg. nafcillin buffered with calcium carbonate. FOR ORAL SOLUTION—Combination pkg. of vial of dry nafcillin sodium as monohydrate and bottle of diluent—provides 80 ml. of solution containing equivalent of 250 mg. nafcillin per 5 ml. Alcohol 2%.

WYETH LABORATORIES PHILADELPHIA, PA.

Giant Fibrovascular Polyp of the Esophagus

David Lolley, M.D., Maruf A. Razzuk, M.D.,
and Harold C. Urschel, Jr., M.D.

ABSTRACT **A case of giant fibrovascular polyp of the esophagus with a review of the literature is presented. The lesion is benign and pedunculated and may attain giant proportions. Symptoms are related to esophageal obstruction. Death by asphyxia can occur. Small lesions can be removed endoscopically with a snare. Larger lesions should be excised using a formal surgical approach.**

Fibrovascular polyps of the esophagus occur infrequently and usually produce symptoms of progressive dysphagia at the outset. They are pedunculated and can attain giant proportions, sometimes exceeding 14 cm in length. Clinical attention is attracted by their bizarre manifestations of dysphagia, nausea, regurgitation, and the tendency to produce sudden death by asphyxiation [2, 5, 8, 12]. The following case is reported to call attention to this rare lesion and to emphasize the need for prompt surgical resection to relieve symptoms and circumvent the possible complication of asphyxia.

A 53-year-old woman was admitted to the hospital with a six-year history of progressive dysphagia, nausea, intermittent regurgitation of digested and undigested food, substernal distress, and gradual restriction of oral intake to clear fluids only. Four years previously she had undergone an upper gastrointestinal series and esophagogram, which had been interpreted as demonstrating a scarred duodenum. However, during all this time she had been having episodes of regurgitation of a fleshy, gourd-sized mass between her teeth, associated with severe respiratory distress relieved when the patient manually reduced the mass into her esophagus. She had managed to conceal this from her family and physicians for years, and only when her husband inadvertently witnessed such an episode was the true nature of her swallowing difficulties disclosed and proper medical attention initiated. She had lost 13.6 kg during this time, but she maintained good health and her physical examination was unremarkable. Work-up included an esophagogram that showed a large polypoid mass attached to the cervical esophagus by a stalk at the level of the cricopharyngeus muscle (Fig 1). Cine esophagography showed the mass to move up and down in the esophagus, at times reaching the hiatus. At rest it assumed a position in the midesophagus.

At operation attempts to snare the stalk of the polyp during esophagoscopy failed because of its firmness and broad base. Surgical resection was carried out through a transverse lower cervical incision and esophagotomy. The stalk was divided with a rim of esophageal mucosa. The latter was repaired and the esophagotomy was closed. Frozen sections of the mass, stalk, and surrounding esophageal mucosa showed no malignancy. Postoperatively the patient had a benign course and was completely relieved of all her symptoms.

Grossly the lesion had a smooth, shiny surface with no ulcerations (Fig 2). Microscopically the tumor was lined by normal-looking, nonkeratinized, stratified squamous epithelium. Its main bulk was composed of vascular fibroadipose tissue infiltrated by chronic inflammatory cells. Scattered foci of ossification were encountered.

Comment

Benign pedunculated fibrovascular polyps of the esophagus are uncommon. Despite early medical interest, only 41 cases have been reported [10]. Characteristically these lesions arise in the upper third of the esophagus, often adjacent to the cricopharygeus muscle [6]. Peristalsis and the molding effect produced by the muscular action of the esophagus have been thought

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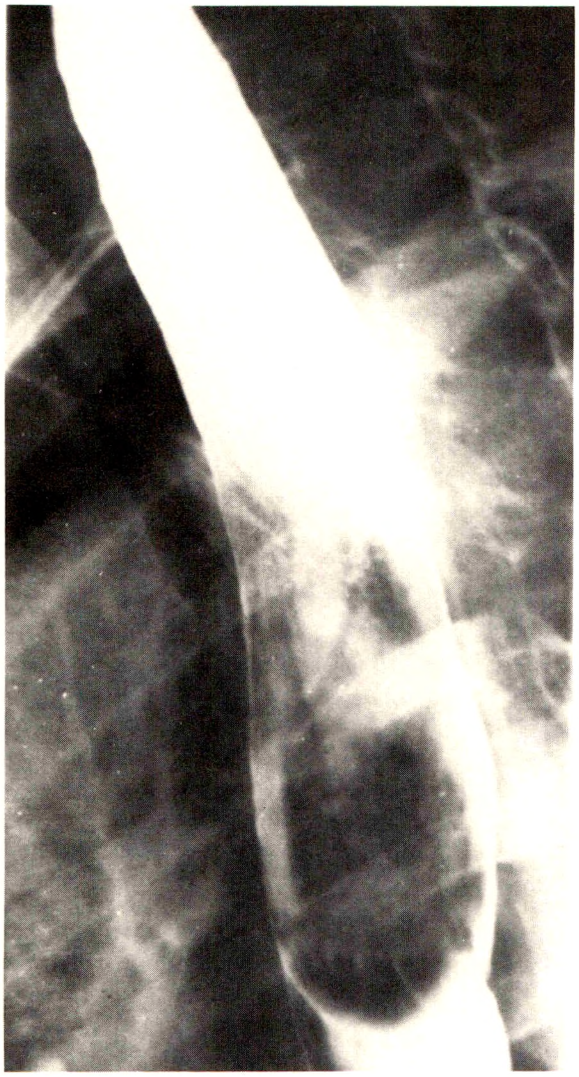

Fig 1. Barium swallow showing filling defect in midesophagus.

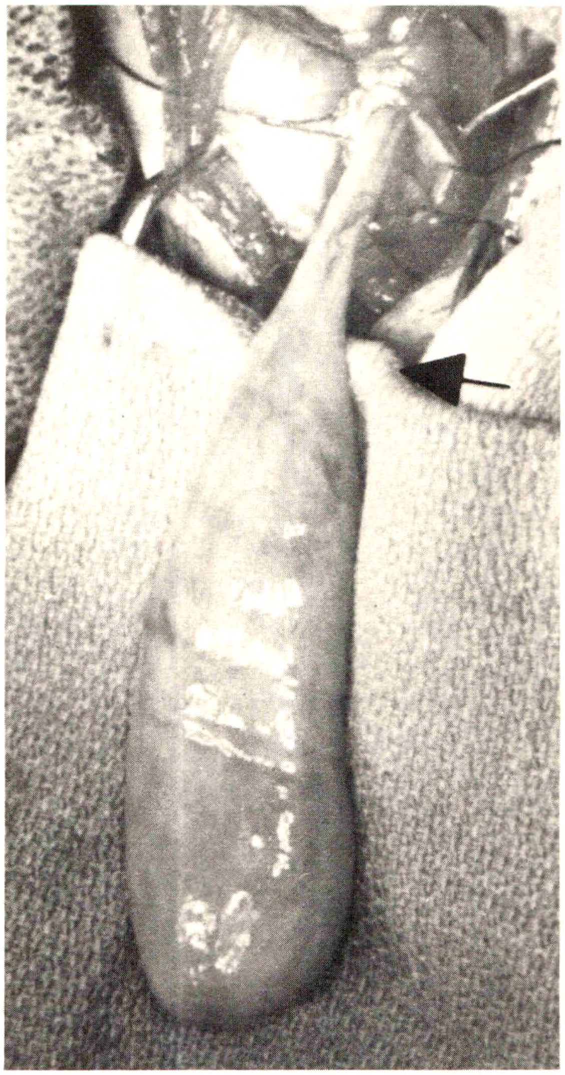

Fig 2. Gross specimen of fibrovascular polyp. The mass is being delivered through the esophagotomy. The stalk is seen to be attached to the esophageal wall.

responsible for the pedunculated shape and giant proportions of these lesions. Symptoms are due chiefly to esophageal obstruction and include dysphagia, regurgitation and aspiration of food, and dyspepsia. Dramatic presentations occur when the mass is regurgitated between the teeth, often accompanied by respiratory distress due to laryngeal obstruction. Sudden death by asphyxiation has been reported [1]. Severe disturbances in nutrition and loss of weight because of interference with dietary intake, significant upper gastrointestinal bleeding due to ulceration of the tumor, and respiratory distress from posterior compression of the trachea by the mass can occur [3, 4].

Characteristically, fibrovascular polyps are seen on barium swallow as a smooth, mobile filling defect that causes forking of the barium stream. This picture can be confused roentgenographically and grossly with other pedunculated tumors of the esophagus including lipoma, myxosarcoma, fibrosarcoma, leiomyosarcoma, rhabdomyosarcoma, carcinosarcoma, and pseudosarcoma.

Small polyps can be removed endoscopically with a snare. However, large lesions (more than 10 cm) and those with a broad base should be removed during a formal surgical procedure, by either a transcervical or transthoracic approach, if the patient's condition permits. This approach affords accurate control of the large vessels in the stalk, which have been reported to be a serious source of hemorrhage when divided by the snare-cautery technique [9]. This also allows a biopsy of the surrounding mucosa to be obtained to rule out malignancy and permits accurate repair of the excision site [7, 11].

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Failure of the Jatene Procedure in a Patient with D-Transposition and Intact Ventricular Septum

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ABSTRACT **Anatomical correction by arterial "switch" procedure was performed in a patient with transposition of the great arteries, intact ventricular septum, and left ventricular hypertension due to distal pulmonary stenosis. The patient died from left ventricular failure. The reasons for the failure of this procedure are discussed.**

Anatomical correction of transposition of the great arteries at the arterial level with coronary reimplantation has been successfully accomplished by Jatene and co-workers [1]. The procedure is thought to be indicated only in the presence of a nonrestrictive ventricular septal defect, because the left ventricular myocardium is then accustomed to pumping against systemic pressure and would be able to support this pressure as the new systemic ventricle.

We have recently seen a patient with transposition and intact ventricular septum in whom left ventricular hypertension was present as a result of distal pulmonary artery stenosis. This case is presented and reasons for the failure of the Jatene procedure are discussed.

A 3-year-old girl was referred from Puerto Rico for elective surgical treatment. The patient had been noted to have a heart murmur at birth and was cyanotic. At 2½ months of age a diagnosis of D-transposition of the great arteries with an atrial septal defect was established by cardiac catheterization (Table). She was placed on a regimen of Lanoxin and followed in clinic. At 8 months of age she developed a neurological disorder, thought to be either meningitis or a brain abscess, that responded to antibiotics. At 2 years 11 months she appeared chronically ill, dyspneic, and cyanotic and was unable to walk. Cardiac catheterization was repeated (see the Table) and showed nearly systemic pressures in the left ventricle with no angiographic evidence of subpulmonic or valvular stenosis, but both the right and left pulmonary artery branches appeared small. Because of her poor general condition she was referred for consideration for operation.

When seen at the Buffalo Children's Hospital on December 6, 1975, at age 3½, she was thin and cyanotic and appeared chronically ill. Blood pressure was 110/70 mm Hg and pulse was 100/min. There was a grade 2/6 continuous murmur at the right sternal border and a systolic ejection murmur at the left sternal border. An ejection click was present, and S_2 was single. No organomegaly was present. Clubbing of the fingers and toes was marked. The electrocardiogram showed sinus rhythm with right bundle-branch block and an axis of plus 180 degrees. The chest roentgenogram showed an enlarged cardiac silhouette and increased pulmonary vascularity. Cardiac catheterization was repeated (see the Table) and confirmed the absence of a gradient across the pulmonic outflow tract and the presence of left ventricular hypertension.

At operation on December 11 the coronary arterial system was found to arise from a single coronary ostium. The anatomy appeared favorable for the Jatene procedure, which was accomplished without difficulty using hypothermia to 20°C and cardiopulmonary bypass with aortic cross-clamping for 45 minutes. The single coronary artery was detached with a portion of great vessel wall, and the resulting defect was patched with Dacron. The coronary anastomosis to the new aorta was carried out by creating a suitable ostium, to which the coronary artery with its cuff of vessel wall was sutured. The great arteries were then divided above the coronary ostium, and end-to-end anastomoses were carried out. After being rewarmed and coming off bypass, the patient developed severe pulmonary edema with elevated left ventricular end-diastolic and left

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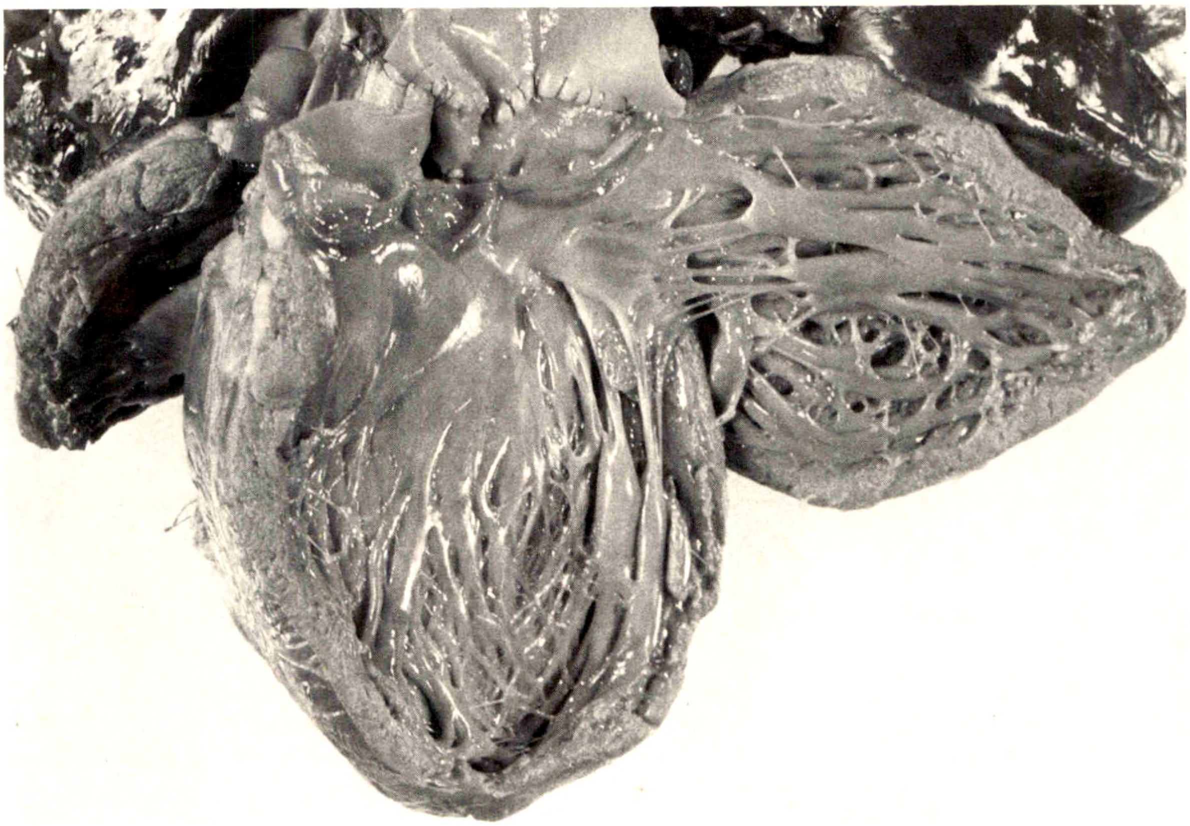
Cardiac Catheterization Data

	Age 2½ mo		Age 2 yr 11 mo		Age 3½ yr	
	Oximetry (%)	Pressure (mm Hg)	Oximetry (%)	Pressure (mm Hg)	Oximetry (%)	Pressure (mm Hg)
SVC	33	. . .	52	. . .	50	. . .
IVC	41	. . .	51	. . .	49	. . .
RA (high)	45	. . .	56	(7.5)	59	(4)
RA (low)	61	(8)	. . .	. . .	. . .	. . .
RV	66	76/0–9	68	82/0–8	67	80/4
Ao	66	76/49	71	80/52	66	80/40
LA	96	(8)	85	(7.5)	87	(4)
LV	89	57/0–9	86	80/6–12	88	50/4
PA	NE	NE	NE	NE	90	50/20
RPA	NE	NE	NE	NE	. . .	15/10
Q_p/Q_s	3.8		2.1		3.2	

SVC = superior vena cava; IVC = inferior vena cava; RA = right atrium; RV = right ventricle; Ao = aorta; LA = left atrium; LV = left ventricle; PA = pulmonary artery; RPA = right pulmonary artery; Q_p/Q_s = intrapulmonary shunt.

Fig 1. The left ventricle and aortic anastomosis opened. A dilated chamber with a thin wall (0.3 cm) is shown. The hypertrophied right ventricular wall (1.3 cm) can be seen to the left.



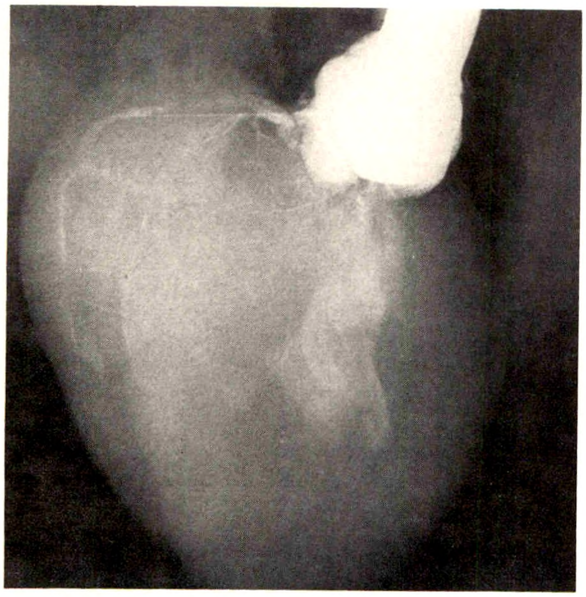


Fig 2. Postmortem flush aortogram. A patent aortocoronary anastomosis is present.

atrial pressure. The pulmonary edema could not be relieved, and she died.

Postmortem examination revealed a dilated and flabby left ventricle with an unexpectedly thin myocardium (Fig 1). The coronary artery anastomosis was patent by angiogram (Fig 2), and no obstruction was present when the coronary vessels were opened.

Comment

Failure of the Jatene procedure in this patient resulted from the inability of the left ventricular myocardium to maintain systemic pressure and flow. This in turn was probably due to insufficient left ventricular muscle mass, since the left ventricular wall was significantly thinner than the hypertrophied right ventricle. We had thought preoperatively that the left ventricle had already been subjected to sufficiently high pressures that it would be able to accomplish the required pressure work as the new systemic ventricle. We perhaps should have realized that our assessment was incorrect because of the inadequacy of pulmonary flow and the two cardiac catheterizations that showed less than systemic pressure in the left ventricle.

The left and right ventricles normally show differences in structure and function that may well be initiated developmentally by the different resistances in the pulmonary and systemic circuits. In transposition with an intact ventricular septum the anatomical left ventricle may develop physiologically as the right ventricle, and in later life the arterial "switch" procedure would impose demands that the left ventricle is not functionally capable of delivering. Anatomical studies of ventricular wall thickness by Shaher [3] and by Lev and colleagues [2] demonstrate declining left ventricular dominance and increasing right ventricular dominance during infancy in transposition with intact ventricular septum.

This raises the question of early correction at the arterial level before the left ventricle has lost its ability to become a functionally competent systemic ventricle. We are hopeful that experimental work may clarify this issue and provide the basis for a justifiable clinical trial. At present, we will reserve the Jatene procedure for patients with transposition of the great arteries and unrestricted ventricular septal defect.

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CURRENT REVIEW

Management of the Patient with a Prosthetic Heart Valve

Francis Robicsek, M.D., and Norris B. Harbold, Jr., M.D.

ABSTRACT **Approximately 20,000 heart valve prostheses are inserted yearly in the United States. Even after successful heart operations, the patients who receive them cannot be regarded as healthy individuals but are a special group with special problems who need close medical attention for the rest of their lives. They are susceptible to many unusual complications because of their implanted foreign body, and it is a challenge to all physicians in contact with them to be aware of their peculiar problems in order to prevent complications if possible and to treat them immediately if they occur.**

General therapy, surgical complications, infection, and mechanical problems are reviewed, with means for management outlined. These difficulties can be dealt with only by careful follow-up and well-coordinated teamwork between the family physician and the institution where the operation was performed.

Evidence suggests that the reason for poor results in most patients who undergo valvular replacement is that surgery was delayed too long. . . .

James R. Pluth, 1974

The development of cardiac valve prostheses has been a gradual process that still has not reached its conclusion. The early artificial valves, which were neither biologically sound nor hemodynamically acceptable, have now been replaced by prosthetic devices of more reliable properties. It has to be realized, however, that even modern prostheses are not free from complications. Patients in whom these devices are implanted can look forward to a life improved in both quality and longevity, but they certainly are not "healthy" individuals. The surgical intervention simply changed their old, severe disease to a new, milder one—a phenomenon common in medical practice. This basic fact of cardiac surgery makes it evident that new methods will have to be developed to cope with these conditions. Unfortunately, this aspect of cardiac surgery has been neglected.

The care of patients with prosthetic heart valves requires four entirely different considerations:

1. General supportive medical therapy
2. Recognition and treatment of surgical complications
3. Monitoring the mechanical performance of the artificial heart valve
4. Prevention and treatment of complications specific to valve prostheses

The performance of these functions should certainly be a joint undertaking of the institution where the operation was performed and the patient's family physician. The sharing of this undertaking, however, may vary widely by custom and by location. In our practice, the patient receives written and verbal advice regarding his diet, physical activities, and medication, and we explain that more detailed instructions will be given to him by his family physician, whom he is to see after his arrival home and who, by that time, will already have received his discharge summary. The patient is given prescriptions to cover the initial period after his discharge in order to avoid confusion and possible duplication of orders. He is made to understand that he is to receive all further medications from his family doctor—a practice we change only at the request of that physician himself.

The patient is seen in the surgeon's office with decreasing frequency, at one week, two weeks, six weeks, and three months postoperatively. After this critical period of possible surgical complications has passed, he is seen by the surgeon only every six months, or any other time his family physician requests. While some recommend readmission and recatheterization of all patients six months after valve replacement as a routine procedure [3], we have not found this

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practice to be indicated in patients who are doing satisfactorily.

As to the frequency of visits to the family physician, that largely depends on the patient's clinical status. A person with compensated single-valve disease that has been corrected by a timely operation may need to see his doctor not more than once every three months except for anticoagulant control. On the other hand, a patient with associated secondary changes, such as cardiac cirrhosis or congestive heart failure, may have to visit his physician every week.

General Supportive Medical Therapy

After his discharge from the hospital—usually on the tenth to the twelfth postoperative day—the patient will still be suffering from the immediate after-effects of a major chest operation. Although he is instructed to "take it easy" for a few weeks, he is also encouraged gradually to increase his *physical activities.* The guideline for the progressive increase is his own judgment and tolerance. The patient is warned to do only whatever does not tire him; by no means should he push himself to the point of exhaustion. A reasonable social and sexual life is encouraged, but he is warned against smoking and the abuse of alcohol. It is explained to him that his prosthetic valve is not a contraindication per se to physical work or to sports. Exactly how much heavy work the patient may do or how much sporting activity he may engage in should be based on his general condition and cardiac status at that particular time, and the fact that he has a prosthetic valve should play only a secondary role. We recommend that a person who has undergone cardiac valve replacement not continue in a profession that involves heavy straining or lifting of great weights, but that he seek employment where less strenuous activity is required. We are definitely against declaring him automatically disabled for life and a ward of society just because he has had an open-heart operation, however. (Children with valve prostheses require a few special considerations which are not discussed in this paper.)

Most of our patients are discharged from the hospital on a *salt-free diet.* This measure is continued for prolonged periods only if it appears necessary in order to maintain the patient in an adequate state of circulatory compensation. Specific diets are also recommended if the patient is overweight, exhibits clinical symptoms of arteriosclerosis, or has an abnormal lipid profile. If he receives diuretics regularly, then the diet is supplemented with liquid potassium chloride in solution; this measure will also reduce the probability of digitalis intoxication.

There is an old axiom that if a patient is ill enough to undergo valve replacement, he is also ill enough to be taking *digitalis.* Some investigators [25, 106] advocate the use of digitalis prophylactically in all patients who undergo valve replacement. We place all patients on digoxin therapy before operation and recommend that they take digitalis for at least a year after the procedure. The patient should take digitalis indefinitely if appreciable cardiomegaly persists or if it is needed to keep him out of congestive heart failure. Digitalis is also the treatment of choice for most types of supraventricular tachycardias. Of these, atrial fibrillation, flutter, or nodal tachycardia respond most favorably, while sinus tachycardia with no signs of heart failure is usually the most resistant [49–52]. Digitalis should also be considered in ventricular tachycardias with heart failure unless digitalis intoxication is suspected. It is our practice to use short-acting digitalis preparations, and digoxin, 0.25 to 0.5 mg daily, is adequate for most patients. Serum levels of digoxin on maintenance dosage are checked before hospital discharge.

We believe it is important for not only the doctor but also the patient to be aware of the symptoms of digitalis toxicity. The patient should count his pulse daily and report to his physician if it consistently drops below 50 at rest or if new dysrhythmias develop. He should also be made knowledgeable about other possible symptoms of digitalis toxicity such as nausea, anorexia, and vomiting. Besides these symptoms, digitalis toxicity could also manifest itself in runs of ventricular tachycardia, bigeminy, and different degrees of atrioventricular block. Paroxysmal atrial tachycardia with heart block and ectopic atrial tachycardia may also occur as consequences of digitalis toxicity [25, 29, 36, 48, 62, 69, 72, 73, 75, 80, 92, 93, 98].

While different types of irregularities in cardiac rhythm are not infrequent in the immediate postoperative period, with the exception of long-standing atrial fibrillation they usually settle before the patient leaves the hospital [2, 27, 33, 45, 80]. Occasionally, however, the administration of *antiarrhythmic drugs* other than digitalis becomes a necessity during the weeks or months following the operation. One of the most frequently used pharmacological agents is quinidine, which is our first choice in the prevention of recurrent atrial tachydysrhythmias or premature ventricular beats [92, 96]. In such cases, quinidine should be administered in doses of 200 to 300 mg. The patient as well as the physician must be aware of quinidine's potential side-effects such as serious dysrhythmias, heart block, nausea, tinnitus, diarrhea, fever, purpura, and skin rash. Other pharmacological agents such as procainamide, propranolol, diphenylhydantoin, and lidocaine are also used frequently during the first few postoperative days, but only rarely after the patient leaves the hospital. Occasionally, however, some of these drugs are needed to suppress ventricular irritability [2, 27, 33, 45, 62, 74, 92, 96, 98].

Two types of dysrhythmias deserve to be mentioned separately. The first is atrial fibrillation that existed before operation and persists in the postoperative period. In such patients we make no special effort to convert the atrial fibrillation into sinus rhythm either pharmacologically or electrically. They are maintained on digitalis and on especially carefully administered anticoagulant therapy and are evaluated no earlier than three months after operation to consider the advisability of synchronized countershock. This is done only if the patient is well compensated and the heart is not significantly enlarged. Electric countershock is performed by the usual well-outlined methods, generally on an outpatient basis, and the patient is kept on quinidine therapy for several months.

The other type of dysrhythmia that merits special consideration if it occurs after valve implantation is that caused by the mechanical effect of the prosthetic cage itself [45]. This complication is most likely to occur in a patient with mitral stenosis and a small left ventricle who received a mitral ball-valve prosthesis. In these patients, the cage of the prosthesis may impinge upon the ventricular septum and serve as a constant focus of irritation. Selecting a mechanical valve of appropriate size may decrease the incidence of this complication, but utilization of a low-profile prosthesis such as the Björk-Shiley valve or the Hancock prosthesis completely eliminates the possibility of this type of dysrhythmia.

The administration of *diuretics* is seldom necessary in the late postoperative period following valve replacement. However, they should not be spared when the patient has poor myocardial function or persistent signs or symptoms of left or right heart failure. In such cases, though, one should also question the technical effectiveness of the prosthesis, and consideration should be given to early hemodynamic reevaluation of the patient's cardiac status. Occasional cases of simple fluid overload, which may require short-term diuretic therapy and salt restriction, are also seen in the first month or so after operation.

Recognition and Treatment of Surgical Complications

Complications of the very early postoperative period such as hemorrhage, acute respiratory insufficiency, and similar problems are not discussed here. It has been our practice to keep the patient in the hospital for at least ten days after operation, during which time those immediate unwanted sequelae, if they occur, can be taken care of. We would like to discuss instead certain events that may complicate the patient's recovery after he leaves the hospital. Some of these problems—such as postpericardiotomy [35, 53, 60, 61, 97] and postperfusion [6, 71] syndrome—are usually self limited. Others, such as infections, could be potential sources of late morbidity and mortality.

Postperfusion and *postpericardiotomy syndromes* are obscure clinical entities characterized by low-grade fever and chest pain as well as occasional splenomegaly and hepatomegaly. In postperfusion syndrome the temperature is usually normal in the morning hours but rises to 37.8° to 39.5°C in the evening [91]. Laboratory studies commonly reveal abnormal liver function studies, high serum glutamic oxaloacetic transaminase levels, and absolute neutropenia with relative lymphocytosis [81, 91]. The disease has been linked to both infectious mononucleosis and serum hepatitis [65, 71, 81]. The current hypothesis [66] is that postperfusion syndrome represents a cytomegalovirus infection that is transmitted in the transfused blood.

Postpericardiotomy syndrome was initially thought to represent reactivation of rheumatic fever [20, 21]. Later came the realization that it can occur in a variety of conditions that may produce pericardial inflammation, such as nonpenetrating trauma and myocardial infarction [35, 53, 101]. Fever and pain are almost invariably present. The liver function and serum glutamic oxaloacetic transaminase values, however, are normal, though the leukocyte count and sedimentation rate are usually elevated [30].

The treatment of both postperfusion and postpericardiotomy syndromes is primarily symptomatic. Chest pain and fever are usually well controlled with rest and salicylates [66], and only severe cases require the administration of corticosteroids [61]. Pericardicentesis may become necessary if signs of tamponade develop [37, 38, 66]. In general, both of these syndromes are self limited and run a benign course. It is important, however, that they be diagnosed to avoid unwarranted treatment for bacterial endocarditis, for which they may be mistaken [1, 5, 23, 26, 28, 31, 34, 39, 42, 44, 46, 47, 54, 55, 67, 76, 82, 85, 88–90, 94, 95, 99, 100, 103–105, 107]. The most important features in the differentiation of both syndromes from endocarditis are: a less toxic course; absence of high-spiking fever; and lack of anemia, petechiae, and peripheral embolization [66]. It is wise to obtain a few blood cultures in all patients to exclude blood-borne or prosthetic infection.

Local *bacterial and fungal infections* are probably the leading postoperative complications [1, 5, 26, 34, 39, 42, 44, 46, 47, 54, 55, 67, 85, 88–90, 94, 95, 99]. They may involve the thoracotomy incision or the groins, if these were used for cannulation. By and large, these local infections seldom constitute a serious threat to either health or life and can be treated adequately by debridement and other topical measures. Probably the most dangerous and certainly the most annoying local infection is one involving the sternum. This type requires broad exposure, drainage, irrigation, and occasionally skin grafting.

Especially dangerous forms of infection are those which invade the bloodstream, because they may easily develop into a full-blown systemic infection with prosthetic endocarditis. These infections are characterized by a toxic course, anemia, high-spiking fever, and septic emboli. To prevent this dread but fortunately rare complication, it is mandatory that the operation itself be done using the strictest aseptic technique and under the protective umbrella of heavy antibiotic coverage postoperatively. In our institution we use cephalothin or ampicillin in large doses, beginning on the preoperative day and carried through the postoperative week. Beyond this period, antibiotics are continued only if a specific reason exists.

In conclusion, while superficial wound infections are not uncommon, serious infections—especially those involving intracardiac structures—are rare; but if they occur, they have to be treated energetically. Naturally, such a course requires hospitalization.

Other problems, though classified as minor, are often of concern to patients and are frequent causes for complaint. The most common is incisional pain. This should be treated with analgesics and reassurance, but angina pectoris must be carefully ruled out in many cases. For this, routine preoperative coronary arteriograms and serial electrocardiograms are extremely useful. Pain caused by late protrusion of a *wire suture* may create an occasional problem. These wires can usually be removed by the surgeon in the office if necessary. *Keloid formation* in the surgical scar is relatively rare, but occasionally it has to be considered for surgical revision.

Monitoring the Mechanical Performance of the Valve Prosthesis

While minor functional imperfections are readily accepted after valvuloplastic operations, modern prosthetic valves are expected to provide a satisfactory opening and near-perfect closure. Signs and symptoms indicating imperfect prosthetic valve function should always be taken seriously.

If the patient's circulation remains well compensated and he has few, if any, cardiac symptoms some six months after valve replacement, this certainly suggests that the implanted prosthetic device is functioning properly. On the other hand, if the patient still exhibits some degree of circulatory impairment, this could be due to one of the following causes.

1. Because the operation was delayed too long, the patient has residual, sometimes irreversible changes in the myocardium or pulmonary vasculature. Characteristically, even these patients show varying degrees of beneficial effects from operation. They continue on a slowly improving trend during the follow-up period until they "level off" at their respective plateau of circulatory decompensation.
2. Whereas one or more defective heart valves were replaced, other significantly damaged cardiac structures—such as other valves or coronary arteries—were left uncorrected. Such a situation may develop either because of faulty preoperative planning or because these additional problems were judged technically uncorrectable preoperatively or at the time of the operation. The clinical postoperative course of this group will often closely resemble that of the preoperative period.
3. Whereas all the necessary corrective measures were indeed undertaken at the time of operation, cardiac structures that had been normal or only slightly abnormal at the time of operation have deteriorated during the intraoperative or postoperative period. Subendocardial left ventricular infarction is probably the most common problem.
4. Last, but not least, the prosthesis is malfunctioning. This should always be suspected if the patient is not doing well after valve replacement. Discounting faulty insertion, which usually manifests itself during the procedure or in the early postoperative period, the cause of the malfunction could be thrombosis, tissue ingrowth, a progressive periprosthetic leak, or wear and tear in the mechanical structure of the valve device itself. Such patients will do well during the postoperative period until their failing prosthetic valve causes either gradually developing cardiac insufficiency or sudden circulatory collapse.

Differentiation among these four classes of unsatisfactory postoperative condition is very important because each requires prompt and energetic medical or surgical treatment or a combination of the two, according to the patient's specific needs. If the cause is worn-out myocardium or surgically inaccessible coronary disease, naturally the patient has to be treated medically. On the other hand, if the peril is surgically correctable, he should be reoperated upon without delay.

The first and most important step in detecting prosthesis malfunction is *evaluation of the patient's state of circulatory compensation by a thorough physical examination.* To do this meaningfully, it is mandatory that the examiner familiarize himself with the patient's past history, his physical and laboratory findings before and after operation, pertinent data about the operation, and the surgeon's prediction of the postoperative results. Serial chest roentgenograms and electrocardiograms are extremely helpful also. It is important, too, that he view his findings in context with previous "check-ups," because one must look not at satisfactory data but at information which truly reflects the patient's changing condition.

Auscultation is naturally a very important part of the clinical evaluation of the patient with a prosthetic valve. After the diseased valve is replaced, the distinct opening and closing sounds of the prosthesis are usually well heard—and each type of prosthesis has its own individual sounds. Though malfunction does not always change these sounds, absence or variations in their intensity or timing or diminution in the opening or closing bruits strongly suggests impediment of the disc or the poppet. The family physician, who sees the patient frequently, is often extremely skilled in detecting changes in prosthetic sounds that have developed since the previous examination.

The presence of an early systolic ejection murmur is a normal finding following aortic valve replacement. This murmur is caused by turbulent blood flow as blood is ejected from the ventricle through the relative stenosis of the prosthetic orifice [56, 66, 102]. However, aortic diastolic murmurs should always be taken seriously because they signify either abnormal seating of the poppet or a periprosthetic leak.

After mitral or tricuspid valve replacement, systolic murmurs rarely occur without appreciable regurgitation through or around the prosthesis. Diastolic murmurs usually signify either a prosthesis that is too small or stenosis in development. Here again, a change in the character of the prosthetic sounds or murmur is more important than the presence of the murmur per se [58, 59].

Phonocardiography has proved helpful in documenting variations in prosthetic sounds or murmurs in some patients. An abnormally late mitral or tricuspid opening sound may be associated with impaired poppet motion, and an unusually early opening sound could be caused by a stenosed mitral orifice. Phonocardiograms are also useful in delineating all the sounds in patients who have two or more valve prostheses [4, 24, 32, 56, 57, 59].

Among the noninvasive investigative techniques, *echocardiography* may also reveal important clues to prosthesis malfunction. Ball-valve prostheses in the mitral position are most suitable for echocardiographic evaluation. Decreased excursion of the ball poppet or sticking or incomplete opening of one margin with "cocking" of a disc can be demonstrated at times with this method [63, 66, 77, 79].

Fluoroscopy can also be helpful in evaluating prosthetic valve function. The poppets of some types of prosthetic valves, such as the recent model Björk-Shiley valve, are radiopaque; thus, their motion can be easily observed. In other valves, the movable part is not visible on roentgenogram but it may cast a "negative shadow" in the streaming blood and thus be recognized. Some malfunctions—such as abnormal mobility of the sewing ring due to broken sutures, broken or bent metallic struts, or a flail calcific homograft valve leaflet—can be seen on fluoroscopic examination alone.

The "ultimate word" in evaluating prosthetic valve function is, naturally, *cardiac catheterization with or without angiocardiography*. Whereas this examination should be strongly considered whenever clinical signs indicate impaired function of the implanted valve device, valuable time should not be wasted on hemodynamic studies when the clinical evidence for malfunction is overwhelming and the need for reoperation is urgent. Catheterization findings that indicate prosthesis malfunction are: pulmonary hypertension with a recurrent significant pressure gradient across the prosthesis; a regurgitant jet of contrast medium through or around the prosthesis; and actual demonstration of the thrombus on the valve as a filling defect on angiography or demonstration of a "frozen" or abnormally moving poppet or disc.

Prevention and Treatment of Late Complications Specific to Valve Prostheses

Although a prosthetic valve is made to last through an expected lifetime, as long as the patient lives it will remain a potential source of complication—the most common being *thrombosis and embolism*, which will hang over his head like the sword of Damocles. The possibility of thromboembolism, present with any kind of prosthetic valve, varies in probability with each patient and with the type and location of the prosthesis. Deposition of thrombus or fibrin on the valve device can usually be prevented by an adequate regimen of anticoagulation. Less frequently, tissue ingrowth can also cause a prosthesis to malfunction, which appears to be an unpredictable problem.

Mechanical failure of the device can also lead to malfunction of the prosthesis. This may vary from slightly imperfect seating to frank ejection of the poppet. The cause of mechanical failure is usually wear and tear of the poppet or the cage struts. Whereas this happened frequently with the early devices, improvement in the material components has made mechanical failure of valve prostheses rare now [3, 4, 7–22, 24, 40, 41, 43, 63, 64, 68, 77–79, 83, 84, 86, 87].

Suspected thrombosis or mechanical failure of a prosthetic valve should be considered an emergency requiring immediate restudy and, if malfunction is present, immediate reoperation. While both thrombosis and mechanical failure require speedy reoperation, small *perivalvular regurgitant leaks* may be followed conservatively. Such leaks may develop because of weakness of the surrounding tissue, faulty surgical technique, improper suture material, or a combination of these factors. Just as improvement in materials has significantly decreased the occurrence of mechanical failure of prostheses, innovations in surgical technique have made perivalvular leak an infrequent complication. If the leak is hemodynamically significant or if it causes severe hemolysis, reoperation for correction of the mechanical defect is needed [40, 41, 43, 56, 57, 59, 63, 68].

Patients with atrial fibrillation or a significantly dilated left atrium are especially apt to develop *thrombosis and embolization.* A prosthesis in the mitral position is more likely to lead to clot formation than one used to replace the aortic valve. Similarly, the make of the device can play a significant role. Some valves—such as the Kay-Shiley disc prostheses and some early types of Starr-Edwards valves—are notoriously thrombogenic, while the Smeloff-Cutter, Lillehei-Kaster, and Björk-Shiley mechanical valves cause thrombi less often. Xenograft prostheses such as the Hancock valve are the least likely to form blood clots.

In the past six years, we have used the Björk-Shiley tilting-disc prosthesis [7–22, 89] as the device of preference for mitral valve replacement [83, 84, 89]. This artificial valve has excellent hemodynamic characteristics and a satisfactory record of durability. Unfortunately, as stated before, even with this advanced type of device, the danger of thromboembolism is not eliminated; therefore, it is our practice to begin anticoagulant therapy in all patients in the early postoperative period. The planning of this therapy must begin even before the operation because the surgical plan itself may have to be changed if a contraindication to warfarin therapy exists. Such a contraindication may be medical, such as ulcerative colitis or a history of bleeding ulcer; or it may be a nonmedical factor such as the patient having an uncooperative attitude, medical facilities being unavailable, or the patient being in a profession which is prone to frequent injuries. If such contraindications exist in a patient needing a mitral valve, we implant a xenograft (Hancock valve) as an acceptable alternative. Because of the excellent track record of the Hancock prosthesis, which now extends for more than five years, we have used this valve during the past year in all our patients who required mitral valve replacement. We maintain these patients on anticoagulant therapy for only three months postoperatively. During this period the sewing ring is expected to become covered with epithelium, and the danger of embolization subsides. As far as the aortic valve is concerned, we do not regard inadvisability of anticoagulation as an absolute contraindication to a Björk-Shiley prosthesis, or to any other currently used prosthetic device, because in the aortic position the prosthesis bears a relatively low chance of thromboembolism. We agree with several other investigators who believe that even with aortic prostheses, anticoagulant treatment is desirable.

The drug of choice in long-term anticoagulant treatment for all patients with prosthetic valves is warfarin. Adequate warfarin therapy is not always an easy task, and it is mandatory that the effectiveness of the therapy be monitored by prothrombin determinations done with appropriate frequency. The prothrombin time must be maintained at 2 to 2½ times the control level (in seconds), and laboratory confirmation should be made at least once every week during the first month and as needed later. One prothrombin determination every two or three weeks on the average usually suffices if the patient is well and stable.

Discontinuation of warfarin therapy, though sometimes unavoidable—such as before oral surgery, childbirth, and similar events—is potentially hazardous [83]. If cessation of warfarin therapy becomes a necessity, the patient should preferably be hospitalized, the drug discontinued, and continuous intravenous heparin started [103], allowing three or four days for the prothrombin time to normalize. The heparin is stopped about four to six hours before the planned operation and restarted again about six hours after the operation. Warfarin is given again orally three to four days after operation, when the patient and the wound are stable, but intravenous heparin administration is continued until the prothrombin time returns to the desired level. (We aim to keep the activated partial thromboplastin time at twice the control level while the patient is receiving continuous intravenous heparin therapy.) Careful monitoring of the laboratory coagulation studies and the wound is very important.

Other methods of anticoagulation, such as the platelet inhibitors aspirin and dipyridamole, are also being utilized in some cases. The usual dosage of aspirin is 1 tablet (300 mg) twice a day; for dipyridamole, 50 mg orally four times daily. These drugs seem to work best in the arterial circulation, and we have been using them together or alone when warfarin has caused recurrent bleeding problems and has had to be discontinued. Another method, used rarely, is "low-dose" warfarin therapy along with one or both of the drugs just mentioned. This type of therapy employs warfarin in an average dosage of about 2.5 mg daily, which usually just prolongs the prothrombin time by several seconds but does not produce any bleeding complications. All these methods are still considered secondary to full anticoagulation with warfarin.

If, despite adequate anticoagulation, repeated episodes of systemic embolization occur and cardiac catheterization has demonstrated prosthesis malfunction, other definite therapeutic measures must be taken. If the patient is in atrial fibrillation, cardioversion by electrical or pharmacological means should be attempted. If embolic problems continue or if the patient returns to atrial fibrillation, reoperation should probably be performed to change the prosthetic valve to a different type, preferably to a xenograft.

Bacterial endocarditis of the prosthetic valve is a dread, but fortunately rare occurrence in our practice. To avoid this potentially lethal complication, antibiotics should be utilized if the patient with an implanted valve prosthesis is to undergo a procedure such as dental work (even cleaning of the teeth), cystoscopy, or any type of surgical procedure, however "minor" (such as ear piercing). We utilize bacterial endocarditis prophylaxis as recommended by the American Heart Association [3].

If the suspicion arises that the patient has bacterial invasion of his prosthesis, he should immediately be hospitalized in an institution where cardiac surgical facilities are available. An effort should be made to identify the responsible organism by blood cultures before antibiotic therapy is started. The blood sample for this purpose may be drawn through a catheter inserted close to the prosthetic valve if peripheral blood cultures are repeatedly negative.

After the organism has been identified and sensitivity studies are completed, the patient should be placed on high-dose intravenous antibiotic therapy for not less than four and preferably a minimum of six weeks, depending on the organism and its laboratory and clinical response. After this period, if there is no further clinical or laboratory evidence of infection, intravenous therapy may be discontinued. The patient can be maintained on peroral antibiotics for up to six months if necessary.

If the patient continues on a septic course despite vigorous antibiotic therapy, consideration should be given to reoperation, including removal of the infected prosthesis, mechanical cleanout of bacterial vegetations, debridement of infected cardiac tissue, and implantation of a new prosthetic valve. Surgical intervention should not be delayed if there are clinical signs indicating that the infectious process has led to impaired function or partial detachment of the prosthesis. Valve removal has been necessary in almost half of the reported patients with valve endocarditis, and it is a procedure of high risk.

After successful implantation of the earlier prosthetic valves, it was not unusual for *hemolytic anemia* to develop, characterized by reticulocytosis, elevated serum lactic dehydrogenase and haptoglobulin, and hemosiderinuria. The cause of this condition was the mechanical shearing stress and turbulence generated by these devices. The newer prostheses such as the Björk-Shiley valve rarely lead to this complication, and if hemolytic anemia does develop, it is usually milder and disappears in a few months, after the rough sewing ring of the device becomes covered with epithelium. Treatment consists primarily of replacing the iron lost in the urine [54] and supporting the increased erythropoiesis with administration of folic acid for as long as the anemia persists. The most severe cases may even require blood transfusion. A special form of "prosthesis-generated" hemolytic anemia occurs in connection with perivalvular leaks [54, 55, 64, 65, 86, 87]. The anemia that results is usually proportional to the size of the perivalvular defect. It can be cured only by reoperation.

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EDITORIAL

Aortic Valve Replacement: The Problem of the Small Aortic Annulus

Charles R. Hatcher, Jr., M.D.

The special problems of aortic valve replacement in patients with a small aortic annulus have been approached in many ways. Originally, small prostheses were made on special order to avoid disparity in size between the aortic annulus and aortic prosthesis. Unfortunately, these small valves were associated with unacceptably high aortic gradients. It became apparent a number of years ago that the ball-valve prosthesis was particularly inappropriate for use in patients with a small aortic annulus.

For a time, the Björk-Shiley and Lillehei-Kaster valves were thought to possess characteristics that would make them the valves of choice for use in such patients, and the tilting-disc valve was accepted almost immediately throughout the surgical world for use in the small aortic annulus. It has also become apparent that prolonged, precise anticoagulation therapy is an absolute requirement with the tilting-disc valve in the aortic position and that, while anticoagulation may significantly reduce the threat of prosthetic thrombosis, it does not abolish the threat of thromboembolism.

Extensive experience has shown the porcine heterograft to be a durable tissue valve associated with an extremely low instance of thromboembolic complications. In general, the heterograft possesses acceptable hemodynamic characteristics, but it is known to be functionally stenotic in smaller sizes. Many surgeons routinely use the tilting-disc valve in patients with a small aortic annulus requiring a 19 or 21 mm valve, utilizing the Hancock porcine heterograft when valves 23 mm or larger could be accommodated. As the advantages of the porcine heterograft grew more apparent with expanded usage, special surgical techniques have become common that permit its use in even smaller sizes.

By far the most widespread approach is that of complete removal of aortic leaflets and calcifications to produce maximum size and flexibility of the aortic root. With care and special effort, an aortic root thus prepared will frequently accommodate a larger prosthesis than was first estimated. If not, the noncoronary sinus may be incised through the annulus and the incision extended to the base of the anterior leaflet of the mitral valve according to the technique described by Blank and his co-workers (p 356, this issue). This gives modest enlargement of annular diameter and frequently permits the next larger valve size to be employed. The resultant aortic defect is, of course, closed with a Dacron or Teflon patch, sutured as needed to the aortic wall and the sewing ring of the prosthesis. This approach should be standard technique when only a slight increase in annular size is required.

In the small number of infants and children requiring aortic valve replacement and in extreme cases of small aortic annulus in adults, more drastic maneuvers are in order. A compromise regarding the type of prosthesis to be used must be considered, and utilization of a tilting-disc valve and long-term anticoagulation therapy certainly constitute a reasonable approach. However, if one feels committed to the use of a Hancock heterograft, the left ventricular outflow tract may be enlarged. Konno and his associates [3] originally described 2 patients in whom the left ventricular outflow tract was enlarged by incision across the aortic annulus and into the intraventricular septum, which was exposed through a right ventriculotomy. Subsequently, our experience at Emory University with this technique in 1 adult and 2 pediatric patients has been presented [2, 4].

Although the technique sounds like a formidable undertaking, it is in reality simple to execute. A longitudinal aortotomy is made and the aortic annulus is incised at right angles between the right and left coronary arteries, closer to the

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right coronary ostium but with adequate aortic cuff to permit secure closure without injury to either coronary ostium. At this point an oblique right ventriculotomy is made and carried down to the aortotomy. The ventricular septum is visualized and incised with scissors (one blade in the aorta and one blade in the right ventricle) as needed to allow the aortic annulus to be expanded to any size desired. Injury to the conduction system from a septal incision in this location is unlikely and did not occur in the 5 patients mentioned above. Utilizing this technique, an adult-sized prosthesis can be employed in a small child and almost any size valve can be employed in an adult. The valve is sewn to the posterior aortic annulus with interrupted sutures in a routine fashion. A diamond or elliptical Teflon or Dacron patch is inserted and the lower half sutured to the margins of the ventricular septal defect, the midportion to the sewing ring of the aortic prosthesis, and the upper portion to the aorta. A triangular patch is then employed to close the right ventriculotomy to avoid compromising the right ventricular outflow tract. One-third of this triangular patch is sutured to the patch closing the left ventricular outflow tract.

Of late, considerable interest has developed about the use of a valved conduit from the apex of the left ventricle to the aorta in certain patients with an extreme degree of obstruction at the level of the aortic valve or annulus. Such an approach is attractive on theoretical grounds, and Dr. Denton Cooley [1] recently presented his personal experience with this technique in 5 patients, concluding that this early experience has been satisfactory. It is possible that such an approach may render earlier techniques obsolete.

Whenever possible, the smaller-sized aortic prostheses of any type should be avoided. Tilting-disc valves such as the Björk-Shiley and Lillehei-Kaster have superior hemodynamic characteristics but require long-term anticoagulation. If the Hancock porcine heterograft is preferred, annulus expansion by any of the techniques mentioned must be part of the armamentarium of all cardiac surgeons.

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Valve Function in Venous Grafts

To the Editor:

The paper "Improvement in Forward Coronary Blood Flow by Using a Reversed Saphenous Vein with a Competent Valve" by Phillips and associates (Ann Thorac Surg 21:12, 1976) presents an interesting possibility: prevention of negative flow in a graft by utilizing a competent venous valve. In order for a venous valve to function, negative flow must close the valve. A venous valve has no effect on forward flow. Figure 2 in the paper is a trace of vein graft flow "distal to the vein valve." This trace shows no positive flow less than 70 ml/min with the valve either "competent" or "incompetent." This is a graphic demonstration that the valve was nonfunctional.

A functional valve could be demonstrated with a flow trace showing a negative flow during part of the cardiac cycle, with the leaflet held incompetent, and zero flow during the same part of the cardiac cycle with the valve competent.

Kenneth L. Kayser, P.E.

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Reply

To the Editor:

We thank Mr. Kayser for his succinct comments concerning Figure 2 in our article. Mr. Kayser points out that absence of positive flow of less than 70 ml per minute demonstrates a nonfunctioning valve.

Analysis of pulsatile flow tracings can be complex and often perplexing. The factors used for analysis of the patterns of pulsatile wave form, according to the pattern-recognition theory, include the following: acceleration duration, flow acceleration, peak amplitude, pulse duration, acceleration pulse volume, mean pulse amplitude, baseline flow, and reverse flow [2]. We theorize that if one were able to alter one or more of these factors favorably, improvement in flow could be achieved. A previous paper [1] demonstrated that use of the rapidly acting vein valve increases the total volume of blood per heart beat in the femoral arterial system of a dog by the amount of blood trapped by the valve.

Negative flow in the true sense of the word does not occur. I believe what Mr. Kayser is probably referring to is reversed flow, and this has been shown to occur in all arterial systems, including the coronary arteries of humans. It is not necessary to have negative flow for valve closure; a flow or pressure gradient is all that is required. I have in fact measured a 2 mm Hg pressure gradient across such valves. That a flow gradient exists is evidenced by the increases in pulsatile and mean flows measured across the valves during the competent vs incompetent phases. The results are significant and are consistently reproducible.

Steven J. Phillips, M.D.

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Valve Competence and Vein Graft Hemodynamics

To the Editor:

This letter concerns the article by Phillips, Okies, and Starr, "Improvement in Forward Coronary Blood Flow by Using a Reversed Saphenous Vein with a Competent Valve," Ann Thorac Surg 21:12, 1976.

I do not think there is any justification for the sentence: "The reversal of blood flow that would have occurred during cardiac systole was prevented by the competent vein valve, as demonstrated by increased mean flow measurements." The phasic flow pattern obtained when the valve was incompetent shows no evidence of backflow at any time during the cardiac cycle. In fact, the systolic flow pattern seems not to be affected by the presence or absence of a competent valve. The explanation that is needed is how valve competency changes *diastolic* flow, since diastolic flow is clearly greater when the valve is competent. It is unfortunate that the authors did not publish tracings showing the effect of valve competence on phasic coronary pressure.

The goal of preventing backflow by using a vein with a competent valve would be especially worthwhile in aortic insufficiency, in which marked retrograde coronary flow is known to occur.

Ronald F. Bellamy, LT COL, MC

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REVIEW OF RECENT BOOKS

Cardiac Arrest and Resuscitation (4th ed)
Edited by Hugh E. Stephenson, Jr., M.D.
Mosby, St. Louis, 1974
999 pp, illustrated, $47.50

Reviewed by Will C. Sealy, M.D.

The fourth edition of this book on cardiac arrest is a testimonial to the dedication that Hugh Stephenson has shown over many years to this important subject. It has been his persistence as well as his scholarship that have led to the worldwide dissemination of knowledge on plans and procedures for recognition of cardiac arrest and resuscitation of its victims.

The strong points in this volume are too numerous to cite. The first chapter, by Negovski of Russia, is excellent and covers the subject of resuscitation and its sequelae unusually well. The sections on organization within the hospital as well as special areas are all well planned and practical. The bibliography is complete and current.

The editor's wish to cover everything about the subject is the major fault of this edition, which now numbers 999 pages as compared to 367 pages in the first edition. In all, it contains eleven parts and sixty-eight chapters, as well as an appendix, an epilogue, and a complete bibliography. The limits of what is meant to be covered under the title *Cardiac Arrest* need to be more precisely identified. Since all human beings eventually experience cardiac standstill, the subject of cardiac arrest could be extended until it became an encyclopedia of medicine. To a minor degree this has occurred, for included in the book are discussions of "stone heart," cardiac conduction injuries from open-heart surgery, cardiac transplantation, cardiogenic shock, resuscitation of the newborn, and exsanguinating hemorrhage. All these problems, of course, are associated with cardiac arrest but not with unexpected cardiac arrest. Unexpected arrest may be a simplified expression of what most believe the subject of this book implies.

A section devoted to elective cardiac arrest is out of place in this work. A chapter in this section recommends deliberate cardiac fibrillation without cardiopulmonary bypass for correction of anomalies of the great vessels. I do not believe many would agree that this is an acceptable procedure. There is too much repetition, a disorder frequently associated with multiauthored books. To give just one example, methods of resuscitation are given in three different places, all essentially the same. It is unfortunate that the copyeditors were not more attentive to detail, for there are several errors in the text, such as "the temperature disappears," "froze-down rats," "multiple cardiac arrests by serum potassium are not rare," and an incorrect number on a figure was noted in one place.

This volume is not in any sense of the word a manual to be placed on a resuscitation cart; however, as a source book, it contains most of the world's information on sudden unexpected cardiac arrests. As its past popularity attests, it will continue to be useful to all who deal with patients critically ill of cardiac disease who are manipulated either with drugs or by physical means, both inside and outside the operating room.

Durham, NC

Recent Trends in Cardiovascular and Thoracic Surgery
Edited by J. B. Borman, M.D.
Grune & Stratton, New York, 1975
222 pp, illustrated, $17.50

Reviewed by Derward Lepley, Jr., M.D.

This small text presents a number of papers from leading centers in the world, primarily on various aspects of heart disease with a small section on lung and esophageal surgery. As with all books of this kind, the statistical evaluation of the results of operations for various lesions is somewhat outmoded at the time of publication. Some of the bibliographies tend to be a bit biased, depending upon the center from which the article originated. A disproportionate number of papers concern congenital heart disease (41 pages) and valvular heart disease (89 pages), with only 40 pages devoted to ischemic heart disease.

In its favor, this volume provides a good deal of information on selection of patients for operation and evaluation of long-term care. It would be a good book for residents who are in training in thoracic and cardiovascular surgery, in spite of the fact that some of the statistical data are outdated. Two good chapters cover topics which are a rarity in the world literature today: blast injuries to the chest and thoracic injuries in war.

All in all, this book is a well-written, international collection of papers on the topic of cardiovascular and thoracic surgery.

Milwaukee, WI

Vascular Surgery
Edited by William H. Edwards, M.D.
University Park Press, Baltimore, 1975
257 pp, illustrated, $24.50

Reviewed by W. Sterling Edwards, M.D.

This fine monograph outlines the latest methods of diagnosis, indications for operation, and operative techniques in the field of vascular surgery. The contributors to the volume represent a spectrum of vascular surgeons, some of whom are true pioneers, some relative latecomers, but all have significant and critical contributions to make to our knowledge. Some of the topics discussed are obviously controversial: whether to use a shunt in carotid surgery, indications for operation in the thoracic outlet syndrome, surgical techniques for subclavian and vertebral stenosis; but in most of the areas covered there is now largely a consensus of opinion. The only chapter not quite up to date is the one on aneurysms. For instance, the greatly simplified technique of handling thoracoabdominal aneurysms described by E. S. Crawford (Ann Surg, May 1974) is not included.

This volume is a valuable contribution that will be particularly useful for young surgeons entering the field of vascular surgery, though it will also be helpful to all surgeons involved in the field.

Albuquerque, NM

Atlas of Surgical Operations (4th ed)

Edited by R. M. Zollinger, M.D., and
R. M. Zollinger, Jr., M.D.
New York, Macmillan, 1975
392 pp, illustrated, $45.00

Reviewed by R. Randolph Bradham, M.D.

The fourth edition of *Atlas of Surgical Operations* by Drs. Robert M. Zollinger and Robert M. Zollinger, Jr., combines the two volumes of the third edition into one volume and includes new techniques in gastrointestinal, intraabdominal, and some peripheral vascular surgery. The atlas is a concise technical reference on standard surgical procedures basically designed for the young surgeon and for the established surgeon who needs to review procedures that he does not often perform. More than 90 operations are described.

The three introductory chapters, "Surgical Technique," "Anesthesia," and "Preoperative Preparation and Postoperative Care," are followed by several plates on surgical anatomy showing the abdominal viscera, inferior vena cava, and aorta. There are five sections: "Gastrointestinal Procedures," "Miscellaneous Abdominal Procedures," "Vascular Procedures," "Gynecologic Procedures," and "Miscellaneous Procedures." The first section is the largest and provides multiple drawings to depict the steps in performing operations such as subtotal and total gastrectomy, abdominoperineal resection, total colectomy, pancreaticojejunostomy, and pancreaticoduodenectomy. The last section includes such operations as radical mastectomy, radical neck dissection, hernia repair, thyroidectomy, and repair of rectal prolapse.

The text for each procedure includes brief sections on the indications for the operation, choice of anesthetic, preoperative and postoperative care, and details for the procedure. The plates illustrating the procedures are well organized, easy to follow, and expertly done. New drawings and text are included on vagotomy, pyloroplasty, enterostomy, tube cecostomy, choledochojejunostomy, splenectomy, resection of abdominal aortic aneurysm, aortofemoral bypass, vena caval interruption, saphenous vein stripping, and shunting procedures for portal hypertension.

This atlas should be available to the surgical trainee and to surgeons in smaller hospitals who are often called upon to do emergency operations that they have not performed before or have done only occasionally. It would also be most helpful to a medical student on the surgical service for reference prior to assisting during an operation.

Charleston, SC

Chest, Heart and Vascular Disorders for Physiotherapists

Edited by Joan E. Cash, F.C.S.P., Dip.T.P.
Philadelphia, J. B. Lippincott, 1975
358 pp, illustrated, $12.00

Reviewed by Richard L. Hughes, M.D.

This is a well-organized and lucidly written text which in the United States will be most useful for physiotherapy trainees. It gives a broad, accurate, but in some areas unnecessarily superficial review of the management of the disorders covered. The language, illustrations, and equipment are all British, but this should not deter an American audience since the principles of management and usage are clearly stated.

The first half of the book deals with pulmonary problems, and American students and therapists will find the chapters dealing with pulmonary physiology, intensive care, and diagnostic techniques somewhat brief and dated. The traditional approaches to chest physiotherapy, however, are well covered and fully discussed. The references are reasonably current and consist primarily of the standard texts. Medical students and physicians, unless they deal with the training of physiotherapists, will find little of value that is not available elsewhere. For its stated audience, however, the book is well worth its modest price.

Chicago, IL

The Assessment and Performance of Implanted Cardiac Pacemakers

Edited by G. D. Green, Ph.D., B.Sc.
London, Butterworth, 1975
214 pp, illustrated, $19.95

Reviewed by Seymour Furman, M.D.

Dr. Green is a clinical physicist working in the pacemaker programs of various hospitals in Glasgow, Scotland. He has contributed to pacemaker technology for many years, and the book demonstrates his interest, competence, and broad range of knowledge in this area.

Nevertheless, defects must be noted. The book is highly specialized and does not impart to the clinician the information necessary to manage patients who have had a cardiac pacemaker implanted. The broad range of pacing and variety of arrhythmias amenable to pacing are not discussed. While four of the five modes of ventricular pacing are mentioned, the descriptions are so brief, and the illustrations so few for two of the modes, that the reader could be led to believe that only ventricular asynchronous and ventricular inhibited (demand) pacing are in use. Atrial pacing, the electrophysiology and hemodynamics of pacing, and the response of the heart are not discussed. The author reveals his basic strength in those chapters which deal with engineering aspects of cardiac pacing. The chapter "Pacemaker Frontal Plane Vectors" is a strong exposition of a technique which his group has almost uniquely championed; it has not made a significant impact in the remainder of the world, and other techniques that are widely used are mentioned sketchily or not at all.

One of the most serious problems of the book is that the author is not a clinician. The use of a cardiac pacemaker, a medical tool, is thus beyond this book. Only six roentgenograms are published, two of lead fractures, and the chapter on radiography (exclusive of the six roentgenograms) is only one page long, inadequate to describe the variety and extent of radiographic analysis during implantation and management of a pacemaker. One of the roentgenograms of a lead fracture is incompletely interpreted. Techniques for implantation are mentioned in the most cursory fashion, and no one involved in pacer implantation could hope to learn anything about the methods involved.

The style is rambling. Casual long-windedness has replaced the conciseness and detail which we have come to expect in books from Great Britain. There is a statistical analysis from the literature of pacemaker work in Glasgow, much of it old. For example, the most recent pacemaker model described is the Medtronic 5841, a unit that was superceded in 1971. No other manufacturers' units are mentioned in any detail. The reader receives no information on the existence of the present Medtronic models or those of any other manufacturer or on the ferment now going on in pacemaker technology concerning new power sources, nuclear pacing, programmability, and miniaturization. These are serious oversights, because the statistical data are obsolete in 1975 and cannot be used as a reference for modern equipment.

The author uses a great many terms of his own manufacture, such as *failed implant life-time* or *unibip electrode-lead.* These terms appear only in his writings and have not achieved widespread acceptance. While an effort at development of adequate terminology is to be applauded, the use of terms that are exclusive to one institution can only be considered idiosyncratic and obstructive to comprehension. Unfortunately, the text is filled with such eccentricities.

The book is valuable for what it does offer but cannot in any way be considered a complete review of the techniques, technology, and management of patients with implanted cardiac pacemakers. Perhaps its single major shortcoming is the lack of a unified goal. It is neither an engineering, a statistical, nor a clinical work on pacing. It tries to be all, but is none.

Bronx, NY

Anatomy: A Regional Atlas of the Human Body

Edited by Carmine D. Clemente, Ph.D.
Philadelphia, Lea & Febiger, 1975
320 pp, illustrated, $24.50

Reviewed by J. L. Ehrenhaft, M.D.

Anatomy: A Regional Atlas of the Human Body, edited by Dr. Clemente, a professor of anatomy, has preserved the superb full-color plates of the original atlases of Professors Johannes Sobotta and Frank H. J. Figge as well as the anatomical drawings by Professor Erich Lepier. This new volume has a minimal amount of explanatory text. It gives the serious student of anatomy who desires further information the opportunity to obtain it through an extensive index that is cross-referenced with *Gray's Anatomy,* the 29th American Edition. The explanatory labels on the illustrations are the English translations of the *Nomina Anatomica.* The pages of this atlas are not numbered, and the index follows the numbers given to the illustrations and plates, which are arranged in seven parts according to anatomical region.

The 38-page section on the thorax contains 58 illustrations with short explanatory texts. The organs are illustrated in a topographic anatomical manner as well as in cross-section. Segmental anatomy of the lungs is well illustrated. The anatomy of the heart is given in detail, and its three-dimensional aspect is easily perceived.

This excellent anatomical atlas preserves the character of the older atlases and presents the subject matter in a concise manner. It is an excellent volume for review of anatomy, and it has a strong visual impact on the reader. It is not appropriate for a first course in gross anatomy but is excellent in combination with a more descriptive text such as *Gray's Anatomy,* to which it is closely tied by the cross-index and with which it should be used by the student who must master basic anatomy.

Iowa City, IA

CONTINUING EDUCATION

Meetings in North America, October 1976–March 1977

October Asian-Pacific Congress of Cardiology, Sheraton Waikiki Hotel, Honolulu, HI, Oct 3–8
Contact: M. E. Berk, M.D., Hawaii Heart Association, 245 N Kukui St, Honolulu, HI 96817

American College of Surgeons, Conrad Hilton Hotel, Chicago, IL, Oct 11–15
Contact: C. R. Hanlon, M.D., 55 E Erie St, Chicago, IL 60611

American College of Chest Physicians, Atlanta Hilton Hotel, Atlanta, GA, Oct 24–28
Contact: A. Soffer, M.D., 911 Busse Hwy, Park Ridge, IL 60068

November Western Surgical Association, Del Coronado Hotel, Coronado, CA, Nov 14–17
Contact: W. P. Mikkelsen, 1127 Wilshire Blvd, Los Angeles, CA 90017

American Heart Association, Fontainebleau Hotel, Miami Beach, FL, Nov 15–19
Contact: W. W. Moore, 7320 Greenville Ave, Dallas, TX 75080

December Air Pollution and Patient Management, sponsored by the American Medical Association, Philadelphia, PA, Dec 3
Contact: Ward Duel, American Medical Association, 535 N Dearborn St, Chicago, IL 60610

Southern Surgical Association, The Breakers Hotel, Palm Beach, FL, Dec 6–8
Contact: W. D. Warren, M.D., Emory University School of Medicine, Atlanta, GA 30322

Future Directions in Cardiac Pacing, sponsored by the International Medical Institute, Santa Barbara, CA, Dec 9–11
Contact: John H. K. Vogel, M.D., 200 E Carrillo, Suite 205, Santa Barbara, CA 93101

International College of Surgeons, Las Vegas, NV, Dec 12–16
Contact: W. A. Houser, M.D., 1516 N Lake Shore Dr, Chicago, IL 60610

January Society of Thoracic Surgeons, San Francisco Hilton Hotel, San Francisco, CA, Jan 24–26
Contact: Walter G. Purcell, 111 E Wacker Dr, Chicago, IL 60601

February Supercourse on Lung Disease, sponsored by the American Lung Association of Louisiana, New Orleans, LA, Feb 7–11
Contact: Hurst B. Hatch, M.D., 333 St Charles Ave, Suite 1504, New Orleans, LA 70130

American College of Cardiology, Philadelphia Civic Center, Philadelphia, PA, Feb 28–Mar 3
Contact: W. D. Nelligan, 9650 Rockville Pike, Bethesda, MD 20014

March Association for the Advancement of Medical Instrumentation, Hyatt-Regency Hotel, San Francisco, CA, Mar 13–17
Contact: Association for the Advancement of Medical Instrumentation, 1901 N Fort Myer Dr, Suite 602, Arlington, VA 22209

American College of Surgeons, Los Angeles Hilton Hotel, Los Angeles, CA, Mar 28–31
Contact: C. R. Hanlon, M.D., American College of Surgeons, 55 E Erie St, Chicago, IL 60611

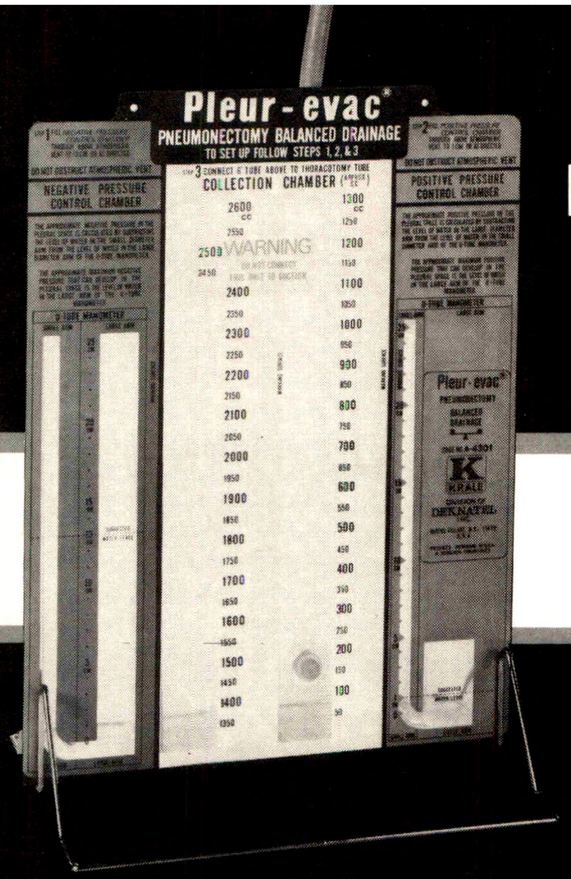
Meetings Outside North America, October 1976–March 1977

October Brazilian Congress on Pulmonary Diseases and Third International Meeting on Pulmonary Diseases, Salvador, Brazil, Oct 24–30
Contact: A. de Souza Machado, M.D., Centro Médico de Graça, Rua Humberto de Campos 11, 11° andar, Salvador, Bahia, Brazil

Third Asian Congress on Thoracic and Cardiovascular Surgery, Sydney, Australia, Oct 26–30
Contact: Ian Monk, M.D., PO Box 378, Crows Nest, NSW 2065, Australia

November Southern Thoracic Surgical Association, Princess Hotel, Acapulco, Mexico, Nov 4–6
Contact: J. Kent Trinkle, M.D., 7703 Floyd Curl Dr, San Antonio, TX 78284

December International College of Surgeons African Annual Meeting, Kampala, Uganda, Dec 1–4
Contact: International College of Surgeons, 1516 N Lake Shore Dr, Chicago, IL 60610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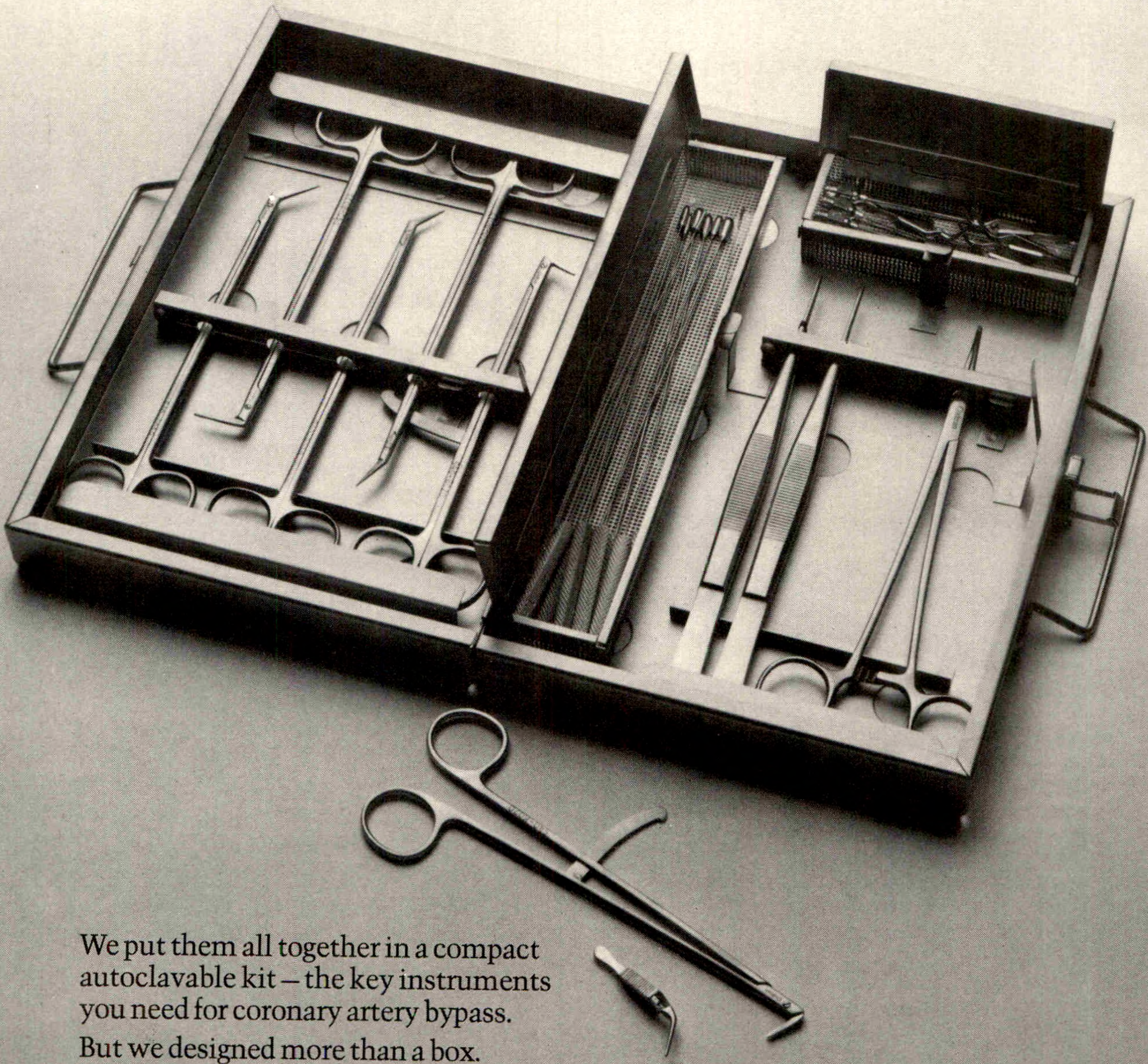

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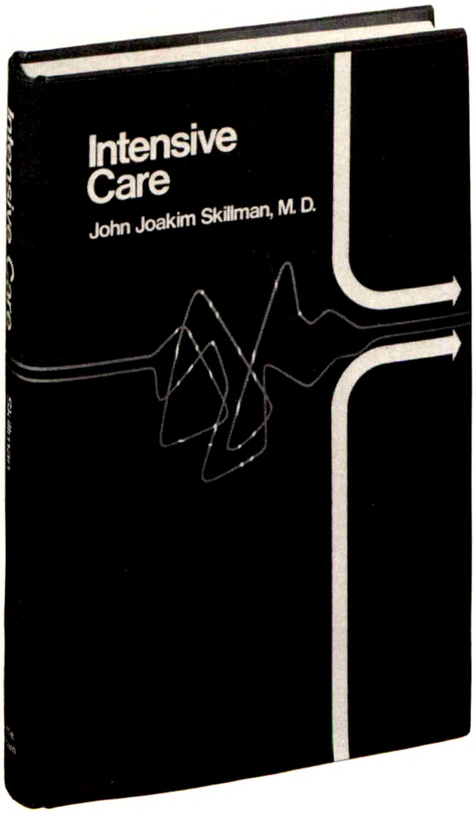

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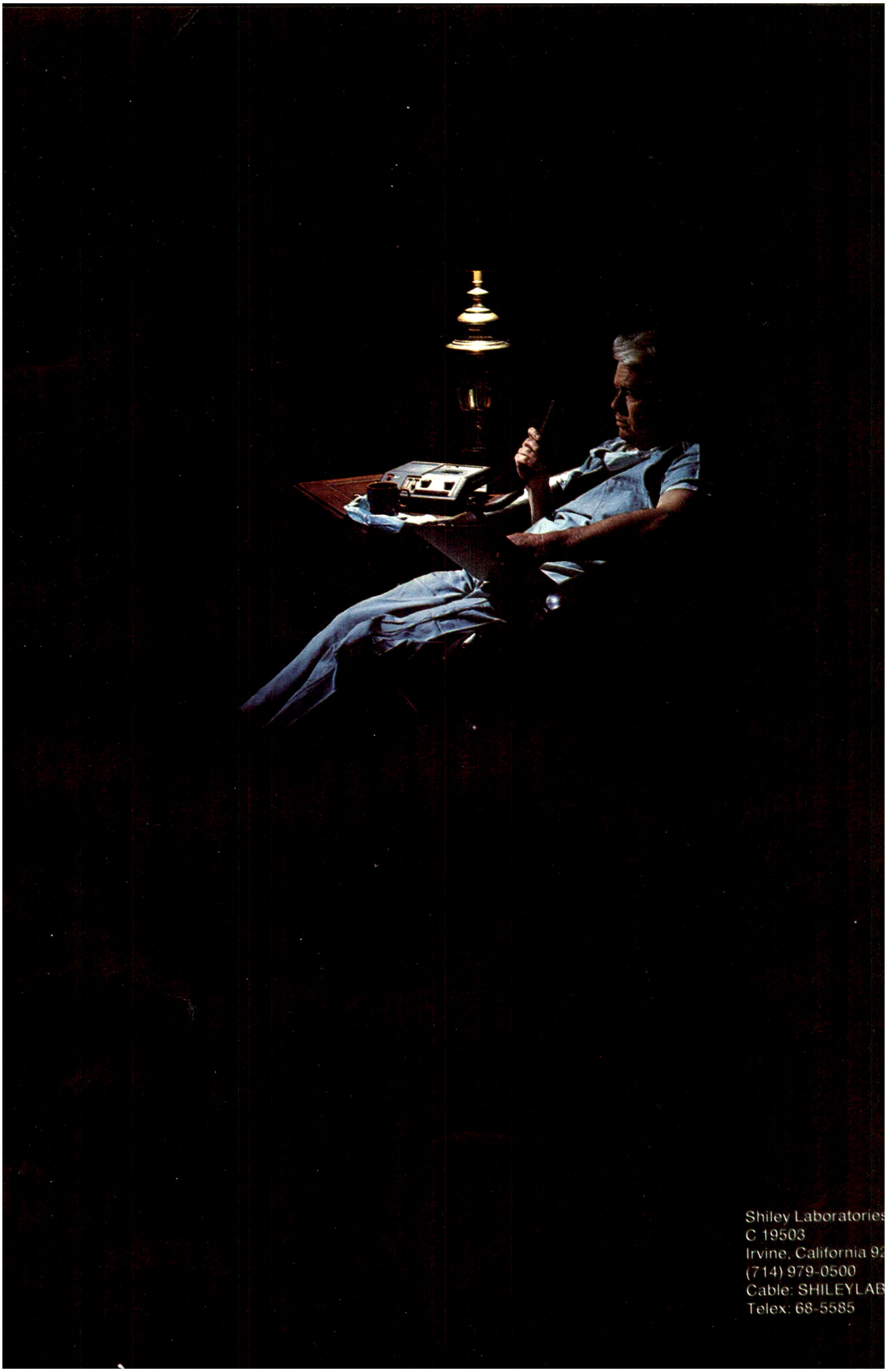

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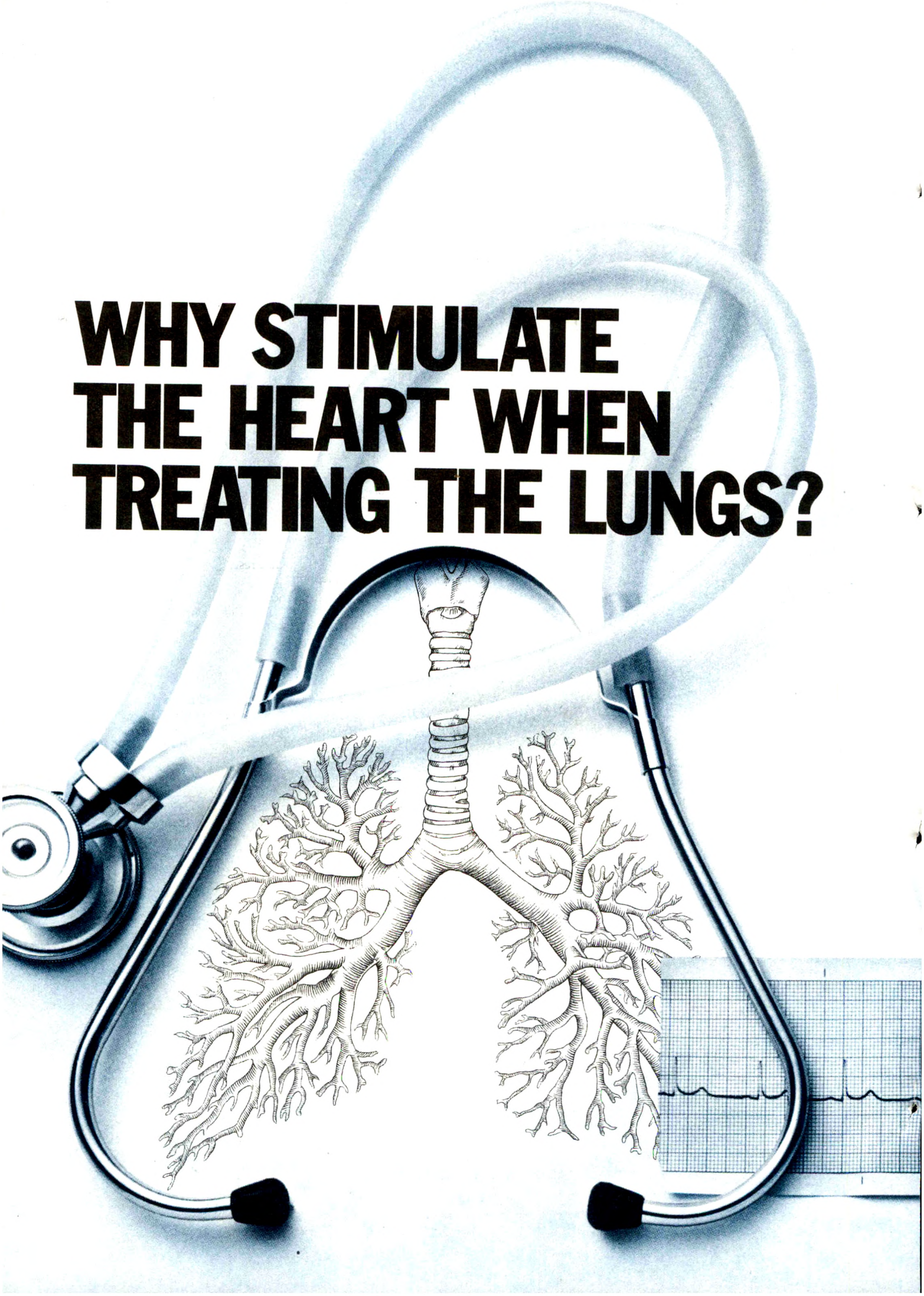

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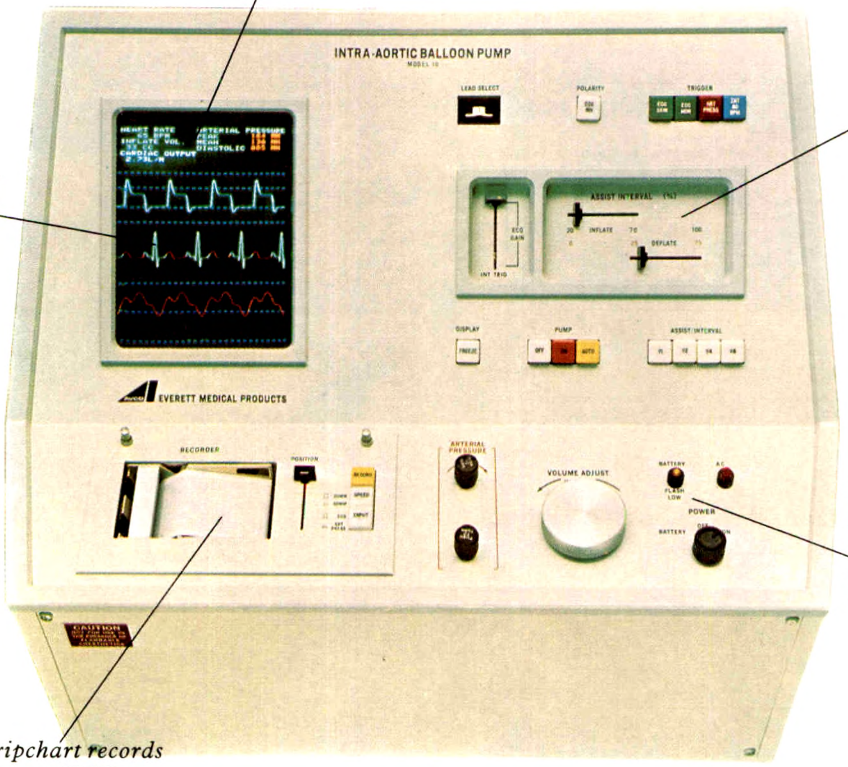

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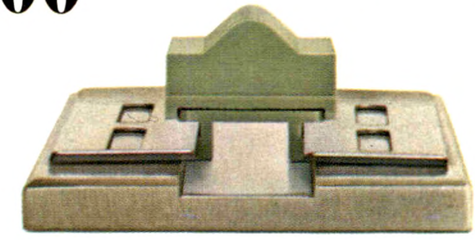

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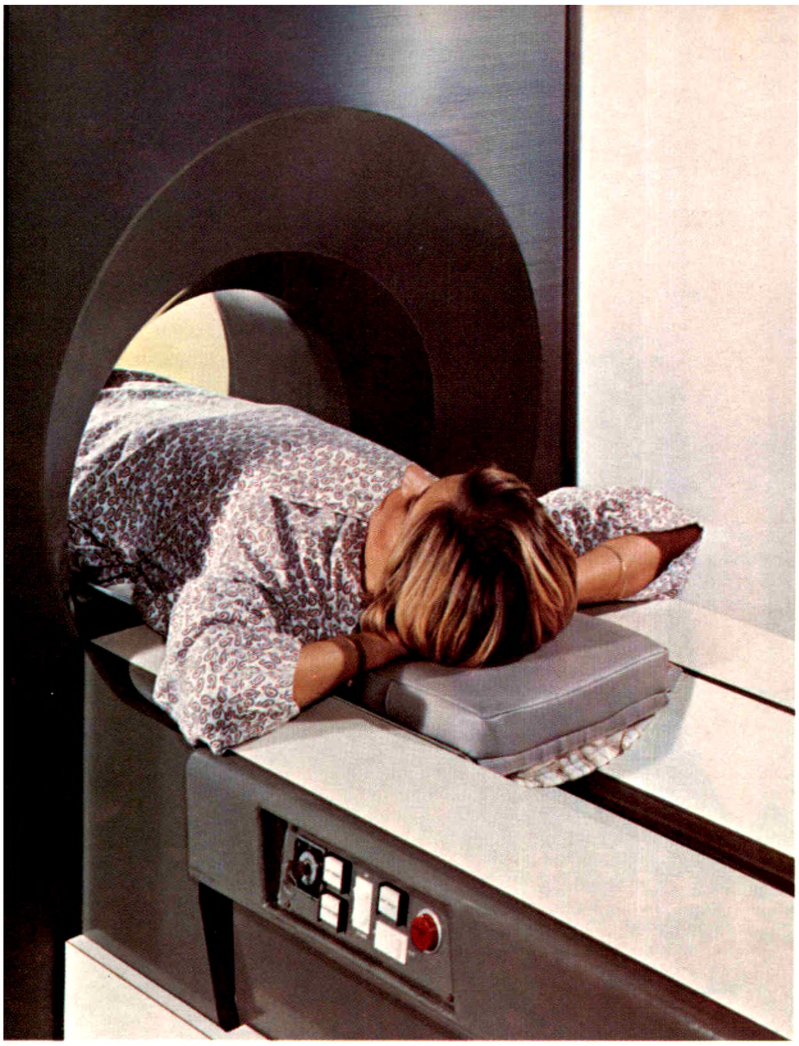

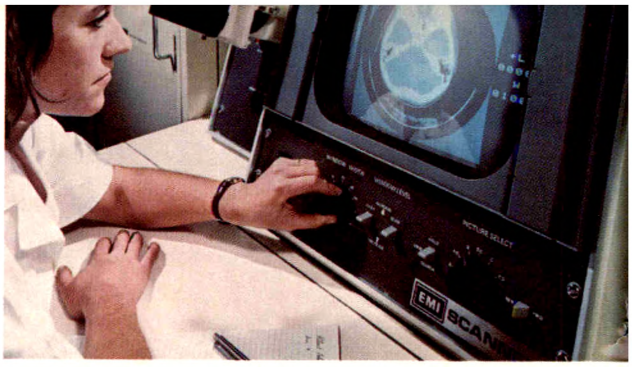

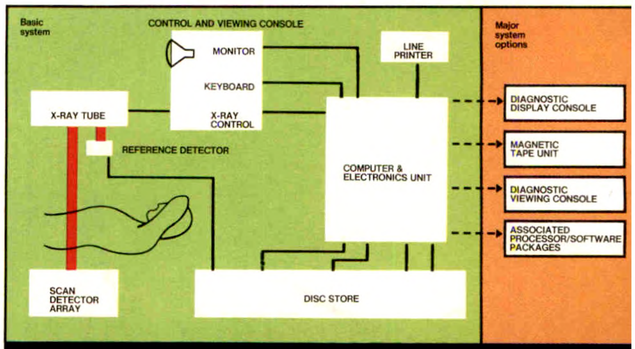

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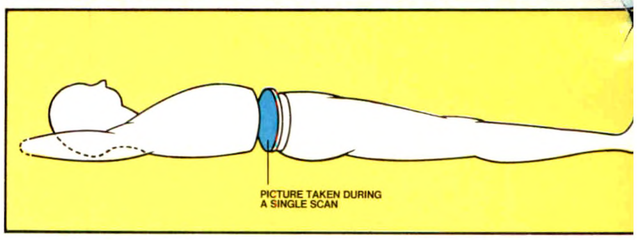
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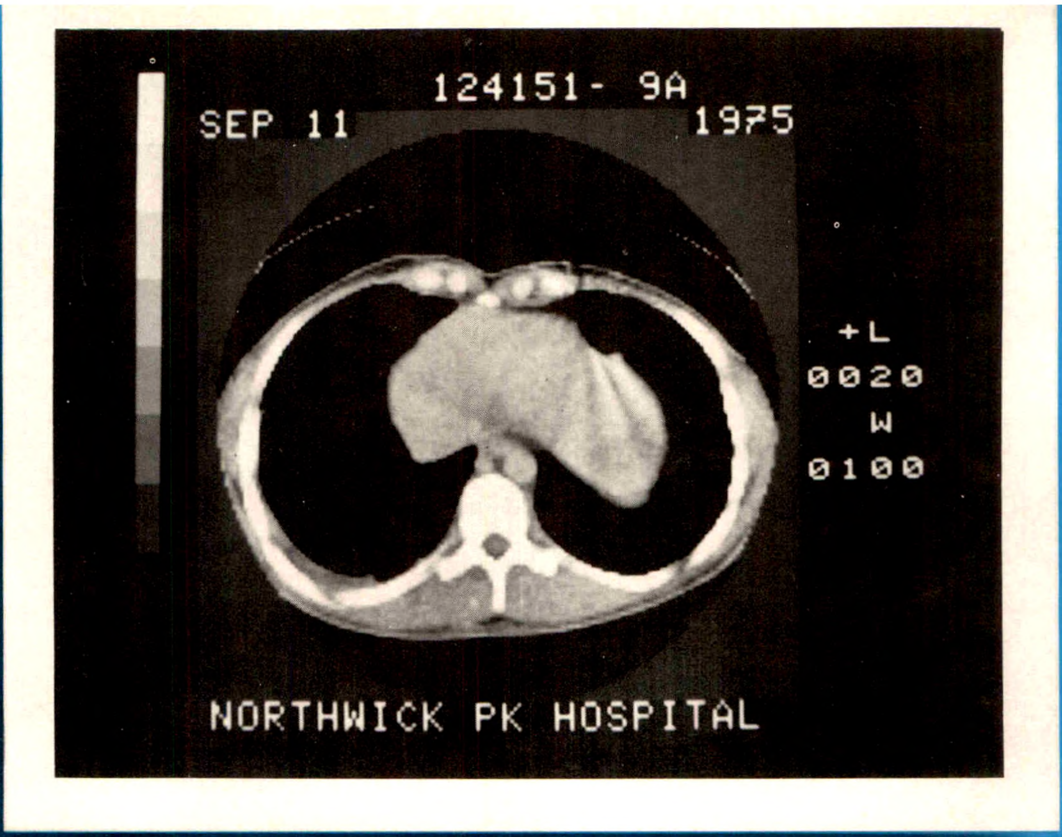

Scan taken at the level of the 10th thoracic vertebra, demonstrating a small pleural effusion on the right side. This was not visible on the standard chest radiograph.

6-218

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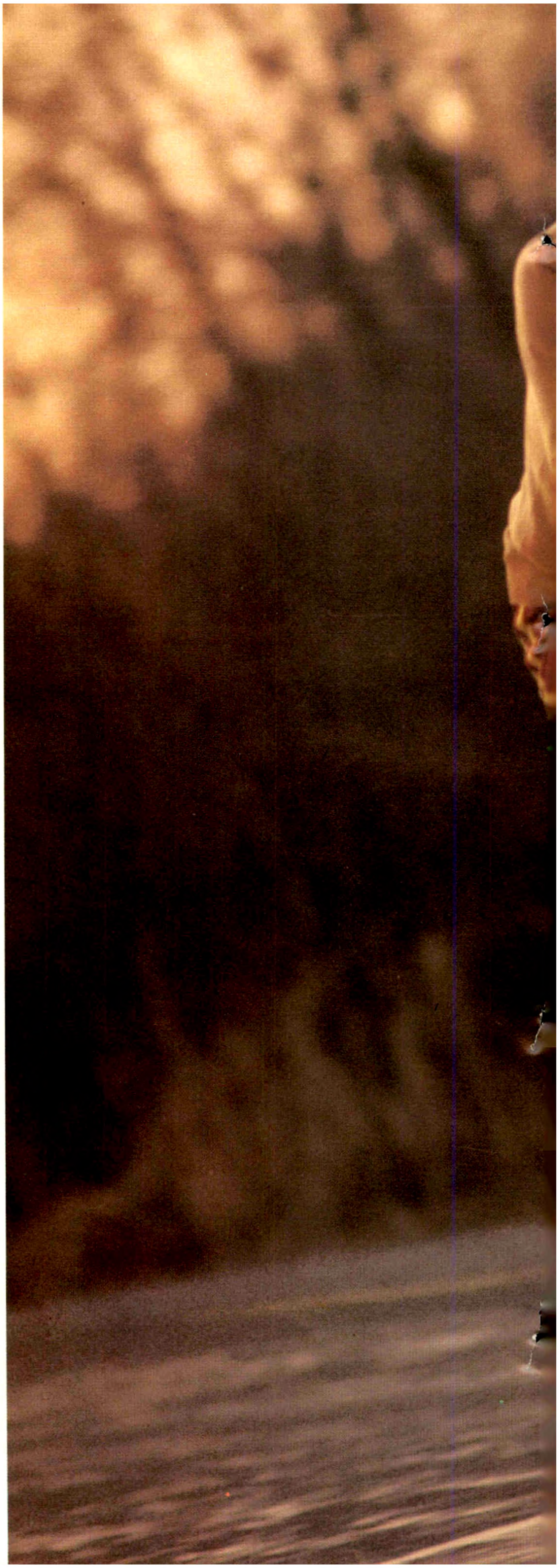

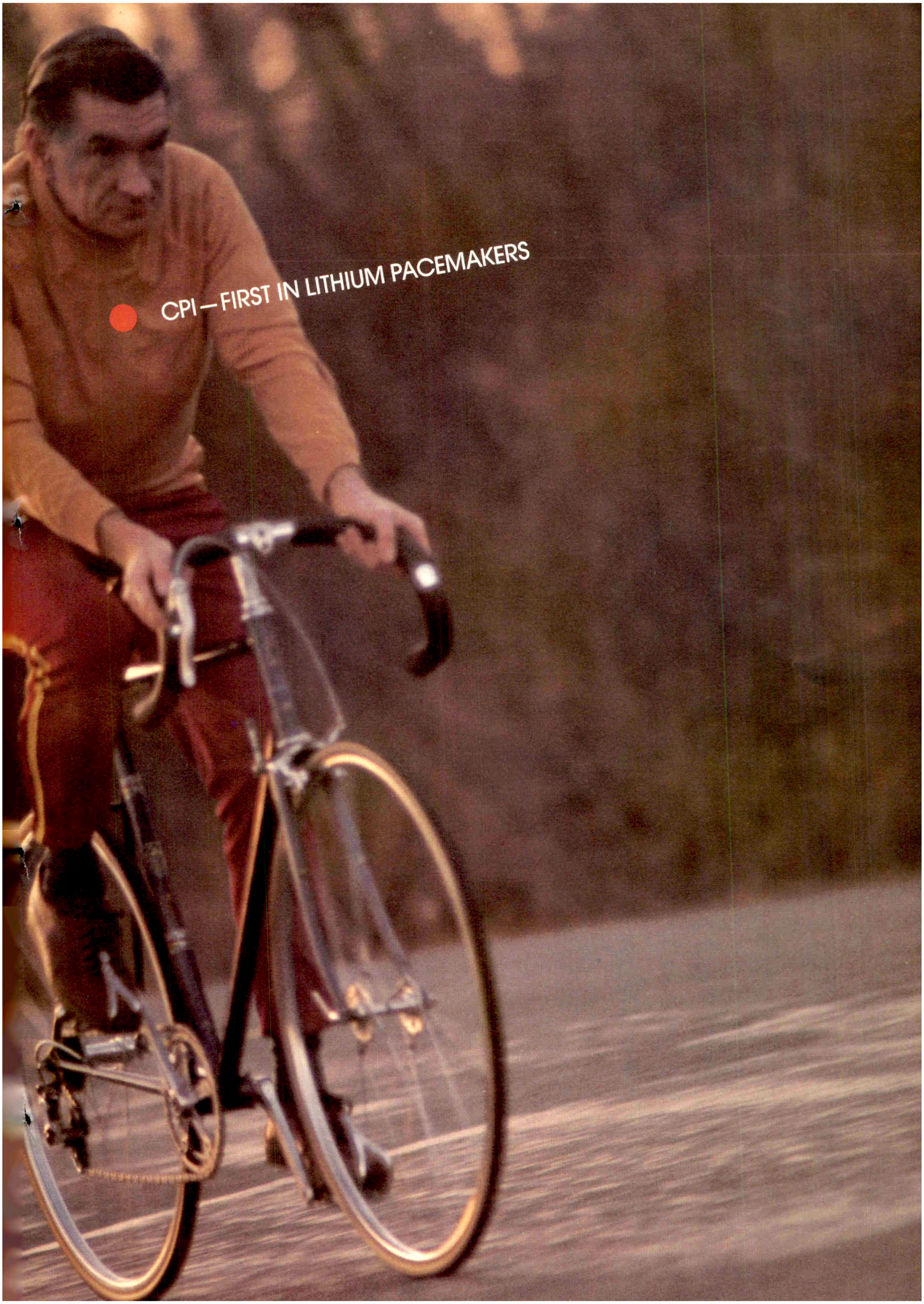

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SIGNIFICANT ADVANTAGES OF THE TEMPTROL Q-200A

CONSISTENT GAS EXCHANGE – The new oxygenation column, which is illustrated in detail on the right, is designed to ensure thorough mixing of the blood and oxygenating gas within the column's center section. This area of secondary flow oxygenation ensures that 95% of all gas transfer occurs within the column itself, and is not dependent upon subsequent oxygenation within a vertical defoaming substructure.

Another plus is the unique design concept, inherent in all Bentley Temptrol Oxygenators, of the 38° incline of the oxygenation column which allows less vertical resistance to the venous return and minimizes the time in which oxygenated blood is exposed to the defoaming material.

LOW PRIMING VOLUME – By decreasing the overall length of the adult heat exchanger by two inches, the minimum blood level has been reduced to 500 ml. This was achieved with no loss of heat exchanger efficiency due to an improved blood flow path around the exchanger.

BUBBLE COLUMN VISUALIZATION – A viewing port has been provided on top of the oxygenation column, where bubble formation and defoaming may be observed.

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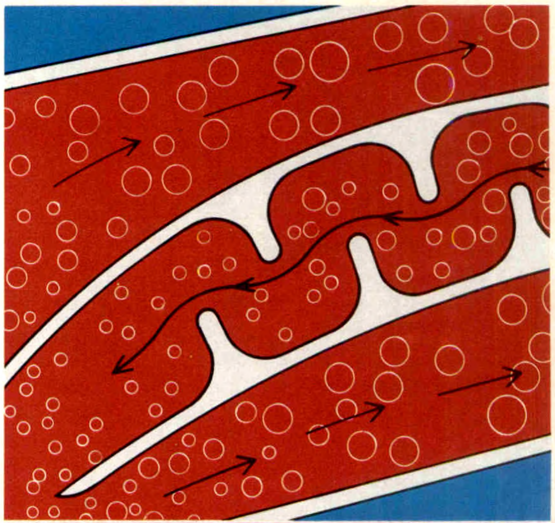
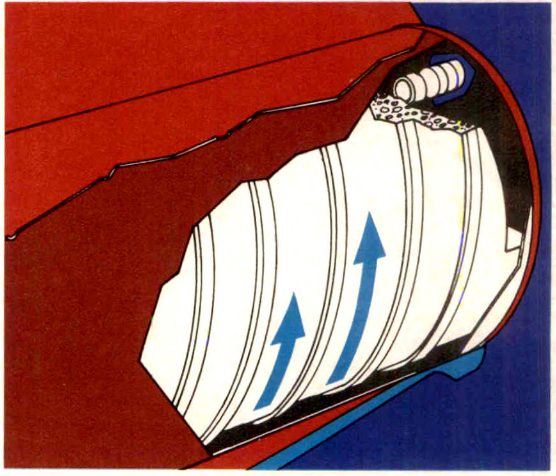
A portion of the Q-200A oxygenation column is illustrated below showing the thorough mixing of blood and oxygen. This secondary flow action, designated by the directional arrows, results in excellent gas exchange over a wide range of adult perfusion rates at extremely low Blood/Gas ratios.





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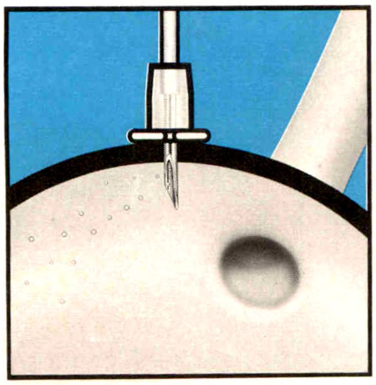
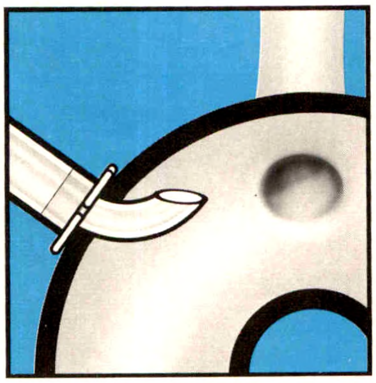


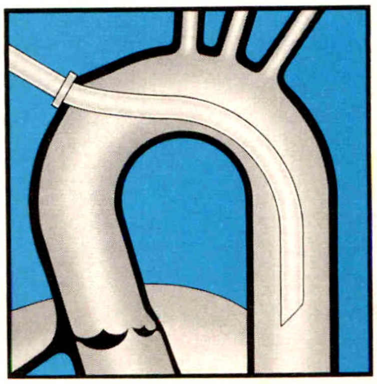
Aortic Vent Needle

Aspirates air from aorta. Stainless steel needle with small flexible tube and tubing connector.



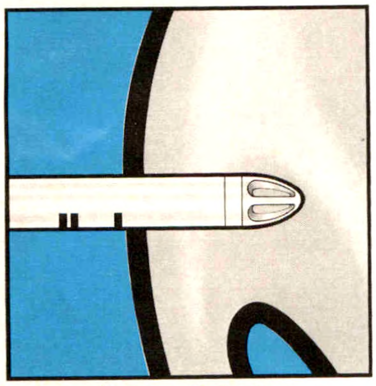
Aortic Arch Cannula

For perfusion of blood into the aortic arch from the heart-lung machine. Full radius plastic tip aligns with blood stream.



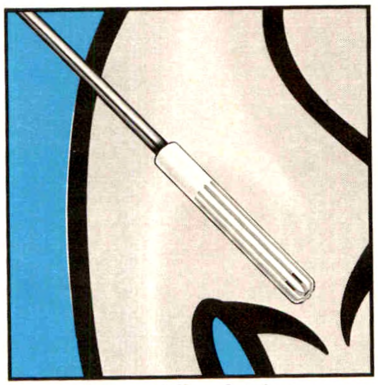
Flexible Aortic Arch Cannula

For perfusion of blood through the aortic arch to the descending aorta. Luer-lok vent aspirates air, removable cap prevents backflow.



Venous Catheter

A single tube method of draining venous return blood when atrium can remain closed, during bypass.



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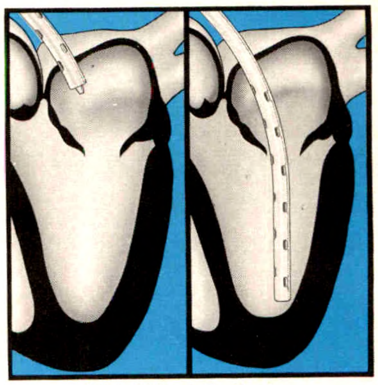
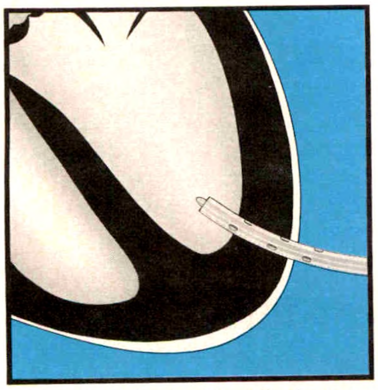
Removes blood from site of operation and returns it to the extracorporeal circuit. Small diameter tip reaches into deep pockets.



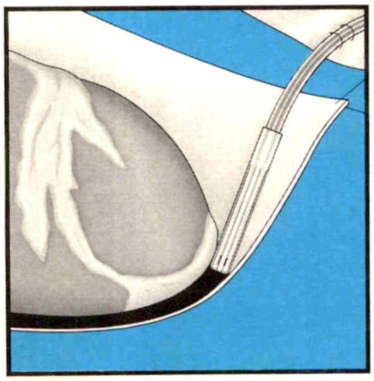
Atrial Vent Catheter

For venting the left heart during cardiopulmonary bypass. The entrance is made through the left atrium and mitral valve.



Left Ventricular Vent Catheter

For venting the left ventricle during cardiopulmonary bypass. Entrance is made directly into the left ventricle.



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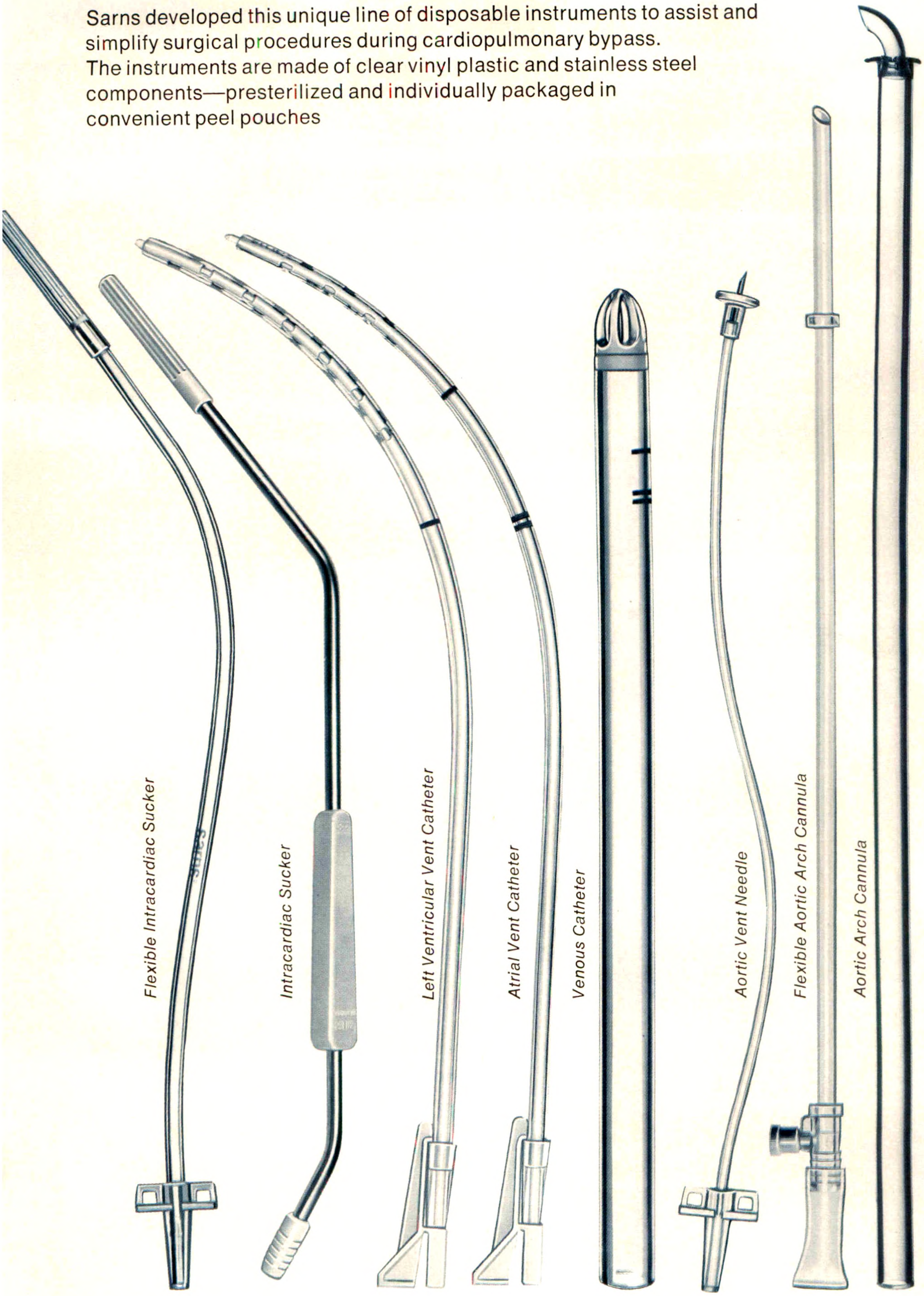
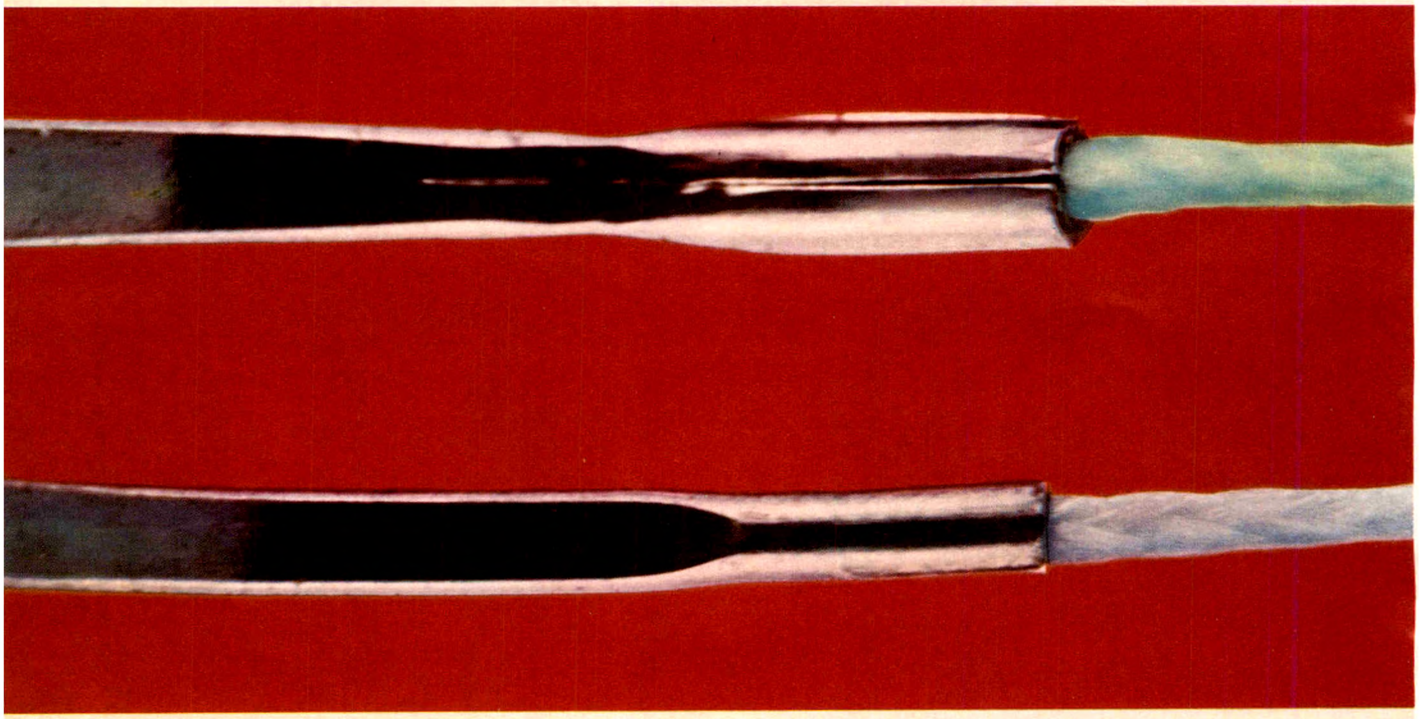


Some polyester sutures with swaged-on needles can spring a leak.



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THE ANNALS OF THORACIC SURGERY Vol 22 No 5 November 1976

The Society of Thoracic Surgeons

Ralph D. Alley, M.D.

ABSTRACT **The opportunity to discuss evolving socioeconomic issues affecting the medical profession as a whole was rejected in favor of personalizing The Society of Thoracic Surgeons for a membership that has grown to almost 1,500 persons. Drawing on historical insights gained through participation in the origin, growth, and development of The Society, I take readers behind the scenes and introduce to them the many people and vast resources that serve our membership. Particular attention is focused on the services of The Society's headquarters office, which is housed and managed by Smith, Bucklin and Associates, Inc, of Chicago, a multiple-association management firm that serves 60 national organizations; on our prestigious publisher, Little, Brown and Company of Boston; and on its link with our Editorial Office in Ann Arbor.**

Even though The Society's Twelfth Annual Meeting was to take place in our seat of government, convened as the first major convention in Washington kicking off the Bicentennial Year, when I reviewed the inventory of potential topics for comment I quickly rejected all issues generic to our profession. For the generic issues, whether they focus on the medical liability crisis, medical manpower, or medical socioeconomics, are best dealt with by the individual state medical societies and their federation, the American Medical Association. Moreover, I did not wish to surge your catecholamine titer by detailing how the Nixon-Richardson Commission on Medical Malpractice, composed of 21 commissioners of whom 12 had law degrees and only 4 had medical degrees, railroaded a voluminous report with recommendations that only make matters worse; or by speculating on the ominous portents for medical education and practice of the medical manpower bills in committee before the Ninety-fourth Congress; or by commenting on the Federal Trade Commission's recent recommendation that physicians and other professionals be permitted to advertise their wares and prices. If there is any doubt about Big Government's pervasive, encircling, and seemingly cynical approach to our profession and institutions, a one-page biopsy should dispel them: Revenue Rule 73-567 of the Internal Revenue Service, which reclassifies American medical specialty boards from educational institutions to business leagues, with attendant adverse tax consequences to the boards. Moreover, the language of the rule is insulting, with vindictive overtones. It is clear that the staff people who prepare these position papers live in a different world, detached from the sick whom we serve on short notice 24 hours a day.

Having exposed my bias on the generic issues, I invite you to pull your wagons into a circle and gather in the middle as a family, not to hear a presidential address, but for a presidential chat. For this will be my only opportunity to share with you some insights concerning the resources of The Society's headquarters office; the publisher of our journal, *The Annals of Thoracic Surgery*; and a few glimpses at how The Society works, illustrated by relevant flashbacks.

History

The Society of Thoracic Surgeons is now twelve years old and is composed of almost 1,500 members. Four years ago in San Francisco, Dr. Robert G. Ellison devoted his presidential address to "Significant Events in the History of The Society of Thoracic Surgeons." This masterful, accurate, and fair-handed exposition of the embryology, birth, and development of The Society was published in our journal (Ann Thorac Surg 14:577, 1972) and should be read by all members who did not hear his inspiring presentation.

During the first five years of The Society's history, while the membership was growing to

From the Division of Cardio-Thoracic Surgery, Department of Surgery, Albany Medical Center, Albany, NY 12208.

Presidential address delivered at the Twelfth Annual Meeting of The Society of Thoracic Surgeons, Washington, DC, Jan 27, 1976.

approximately 700, the administrative and clerical work was carried on by our officers and committee chairmen without financial support. The majority of the work fell upon the Secretary, Dr. Francis X. Byron; Treasurer, Dr. Robert G. Ellison; Editor, Dr. John D. Steele; and Dr. Adams Cowley, Chairman of the first Membership Committee, who sorted out the Founders Group and processed several hundred candidates for membership. A great debt is owed to these gentlemen, to their office personnel, and to the facilities of their institutions for what was essentially a "free ride" during this period.

The amount of work required of the Secretary's office was brought into sharp focus when, after the untimely death of Dr. Byron in the Spring of 1968, Dr. John N. Briggs shouldered the task in preparation for the upcoming Fifth Annual Meeting in San Diego. Soon after The Society's files arrived in Dr. Briggs' office in Encino, California, his secretary resigned. Over the ensuing eight months he lost three additional secretaries, and I suspect this experience played a role in his decision, after the San Diego meeting, to move his office 3,000 miles to Naples, Florida. It was certainly an eye-opener for me, and with my instinct for survival sharpened, I was prepared, when the Nominating Committee offered me the secretaryship commencing with the San Diego meeting, to demand as a precondition to acceptance that a formal headquarters office be established. This was approved by the Council prior to the election.

Headquarters

Having made the demand for a professionally staffed headquarters office, I was of course immediately appointed chairman of a committee to see that this came about. With the help of the other committee members, Drs. John N. Briggs, Robert G. Ellison, and Herbert Sloan, with an assist from Councillor Hiram T. Langston, the decision was made to engage the services of a multiple-association management firm rather than renting an office and hiring our own staff. The field was researched, and within two months of the San Diego meeting a letter of agreement had been signed engaging the services of Smith, Bucklin and Associates, Inc, of Chicago.

Fig 1. The Society headquarters is housed on the sixth floor of this building, known as One Illinois Center, at 111 East Wacker Drive, Chicago.

At the time these arrangements were made in the Spring of 1969, Smith, Bucklin was providing association management services for 37 national organizations headquartered at 333 North Michigan Avenue. Since then, their roster of associations has grown to 60, the largest of which—the National Association of Bank Women—has a membership of 22,000, and the firm has moved to larger quarters at adjacent 111 East Wacker Drive (Fig 1). All but two of the associations managed by Smith, Bucklin are industrial, commercial, or other nonmedical groups. The other medical association is the American College of Nuclear Physicians.

The advantages of employing a multiple-association management firm to serve our Society are numerous. The burdens of renting office space, employing a full-time executive director and supporting clerical staff (of unpredictable turnover), purchasing office furnishings and equipment, and farming out production paperwork to suppliers of uncontrolled reliability are avoided. Our basic fee for access to the vast resources of Smith, Bucklin and Associates and the assignment of Mr. Walter G. Purcell (Fig 2), a Vice-President of Smith, Bucklin, as our account

Fig 2. Walter Purcell in his office preparing the technical exhibit space allocations for this meeting.

Fig 3. Betty Perkins reassuring an anxious author that the abstract of his paper arrived before the deadline.

executive is small and represents but a portion of Mr. Purcell's salary. This fee covers a retainer for his services and those of a back-up executive in the event of his illness as well as office space and utilities. All other services, including stenography, clerical work, accounting, dues billing, preparation and mailing of printed material, and convention management services, are purchased as used. Though we have no full-time personnel, Smith, Bucklin has 85, and they and the resources they provide are available to us on an à la carte, highly professional, and personalized basis.

We are indeed fortunate to have Wally Purcell as our Business Manager. Prior to joining Smith, Bucklin, he was an instructor in the School of Communication Arts at the University of Notre Dame and an executive at the NBC television and radio stations owned by Notre Dame. A true professional, he fits comfortably into the family of The Society of Thoracic Surgeons.

Miss Betty Perkins (Fig 3) is Wally Purcell's Executive Assistant and is as skilled in the art of association management as anyone. Prior to her present role she was secretary to Mr. William Smith, Chairman of the Board of Smith, Bucklin. She is familiar to you as the person who orchestrates the convention bureau personnel at the registration desk at our annual meetings.

Mr. Charles E. Swingley, controller and treasurer at Smith, Bucklin, runs the Accounting Office, makes sure The Society's dues are collected on time, supervises our books of account, and prepares our financial statements for audit. When Bob Ellison was treasurer, typical of a gentleman from the Old South, he wrote personalized, courteous, and most gracious letters to dues delinquents, embellished by inquiries about the health of their families and associates. That service is no longer available, as—fortunately—very few of you have reason to know.

In addition, Smith, Bucklin is able to provide expert graphics and production in their large and impressive production department. They produce and handle thousands of individual printed pieces every workday for the associations they serve. (Smith, Bucklin is said to be the second largest individual mailer in Chicago's zip code 60601, in the heart of the business district.) When Wally Purcell and Betty Perkins prepare a report for our members—anything from a one-page announcement from our Secretary, Tom Bartley, to a fancy printed piece like the flyer for the Women's Program of the 1976 meeting—it can be in the mail the same day if necessary. The sophisticated office equipment used by Smith, Bucklin bears little resemblance to the mimeograph that Frank Byron used to borrow from the City of Hope hospital record room. Fully automatic, it makes a paper plate from an original, duplicates in preset quantities, collates multiple pages, stops automatically, and then begins the next job. It can turn out 10,000 copies per hour. Clearly, whatever the communications needs of present and future committees and officers of The Society may be, they can be met in house at our own headquarters.

Committees

Our Secretary, the Council, and the various committees also handle a great deal of business for The Society. They work throughout the year by correspondence, with occasional meetings, and with staff support from the headquarters office whenever needed. To illustrate, the Standards and Ethics Committee (Fig 4) and the Program Committee (Fig 5) are shown at work last fall in preparation for this meeting.

Fig 4. The Standards and Ethics Committee, under the chairmanship of Dr. F. Henry Ellis. The picture is obviously posed, because they have little to smile about and a tremendous burden of work throughout the year—a necessary but regrettable investment of time on the part of such important clinical thoracic surgeons. Left to right, Dr. Harold V. Liddle; current President, Dr. Thomas B. Ferguson; Dr. Hassan Najafi; Secretary, Dr. Thomas G. Bartley; Chairman Ellis; Dr. W. Sterling Edwards; and former Presidents, Drs. Benson B. Roe and Donald L. Paulson.

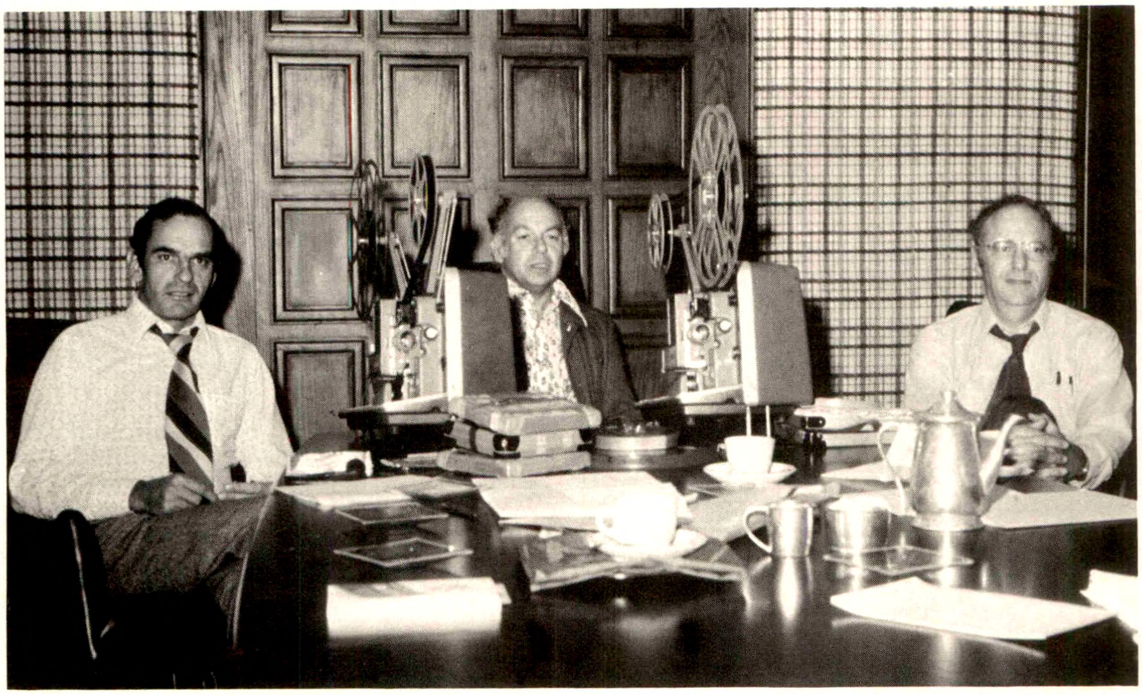
Editor

Dr. Herbert Sloan, Editor of our journal, *The Annals of Thoracic Surgery*, sits in as a consultant to the Program Committee and sometimes spots the abstract of a paper that has been rejected by *The Annals* or has been published somewhere else. It is not sufficient to mention Dr. Sloan in passing. Our Past President is the third director of the John Alexander School of Thoracic Surgery in Ann Arbor, Secretary-Treasurer of the American Board of Thoracic Surgery, and one of its representatives to the American Board of Medical Specialties—in short, a dedicated public servant to our specialty who does something for all of us each and every day.

Dr. Sloan is assisted at the *Annals* editorial office by Administrative Editor, Mrs. Jeanne Tashian. In collaboration with our Editorial Board, Dr. Sloan and Mrs. Tashian set the stage for our elegant journal (Fig 6).

Publisher

Dr. Sloan's office works closely with the publisher of *The Annals*, Little, Brown and Company



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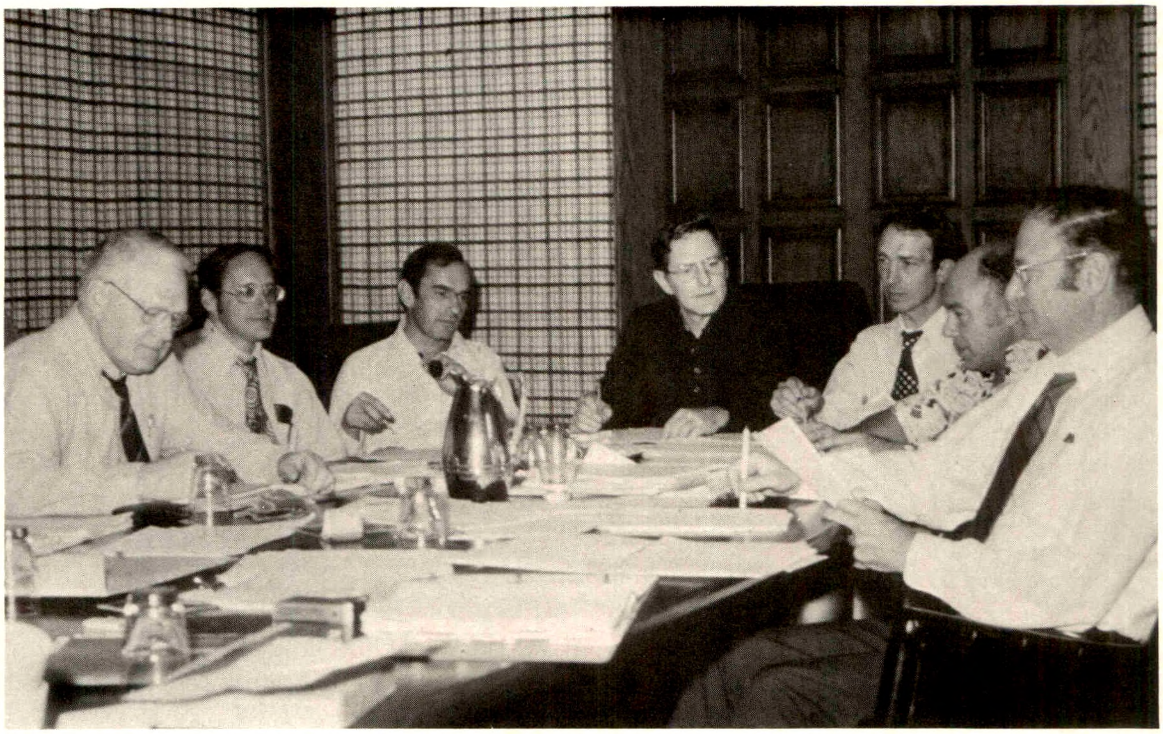

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Fig 5. The members of the current Program Committee assembled in Chicago on the weekend of October 3 to 5, 1975, to make the final selection of abstracts and films. (A) A bank of projectors facilitates the laborious task of movie selection. Note Dr. Jack Greenberg, fresh from Miami and not yet acclimated, flanked by Drs. F. Griffith Pearson and George Robinson. (B) By the next day Dr. Greenberg is seen diligently at work in full floral splendor, flanked by Dr. Gordon Danielson and the hardworking Chairman, George Robinson. The rest of the committee are, left to right, Dr. Herbert Sloan, Editor; Dr. Marvin Kirsh; Dr. Pearson; and Mr. Purcell.

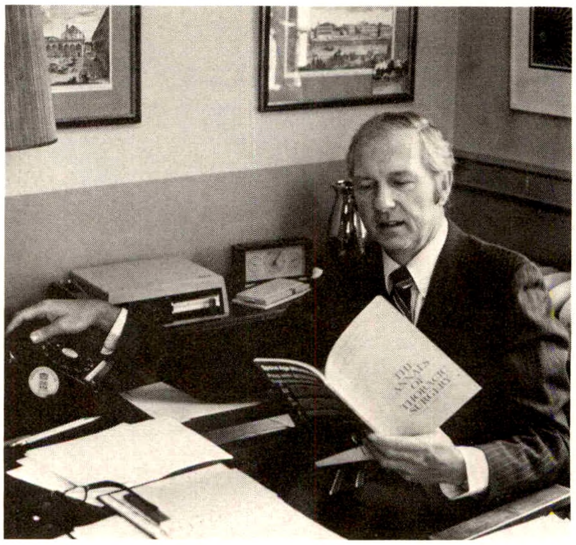
Fig 6. Dr. Sloan and Mrs. Jeanne Tashian of The Annals of Thoracic Surgery *Editorial Office in Ann Arbor.*

Fig 7. Little, Brown and Company, publisher of The Annals of Thoracic Surgery.

of Boston (Fig 7). Whenever I think of their handsome headquarters at 34 Beacon Street, overlooking Boston Common, my thoughts flash back to the first meeting of the Council on a Christmas Holiday weekend in St. Louis. Dr. John D. Steele had been selected as Editor of the proposed *Annals of Thoracic Surgery* at the original Founders Meeting in San Francisco the previous October. Because of his wide acquaintanceship with publishing houses, he had thought there would be no difficulty signing up with a publisher in time to have the initial issue of *The Annals* on display at the first meeting of The Society in January, 1965. To his dismay, all the publishers he contacted but one declined, stating that The Society should prove its viability first. The only publisher interested demanded a $45,000 advance escrow fund for use against potential losses. This company was not Little, Brown.

For since Little, Brown and Company's Medical Book Division did not publish a medical journal, John Steele had not contacted them. I suggested that this was the best reason to approach Little, Brown, and Dr. John Strieder of Boston was assigned as our emissary to make the overture personally. On a parallel track, I telephoned Fred Belliveau, a Vice-President of Little, Brown and General Manager of its Medical Book Division, to assure him that the new society would be successful. A five-year contract with Little, Brown and Company to publish *The Annals of Thoracic Surgery* was signed three months later. This contract was overly generous

Fig 8. Fred Belliveau, Vice-President of Little, Brown and Company, publisher of The Annals of Thoracic Surgery.


THE ANNALS OF THORACIC SURGERY

to The Society, for we shared in the advertising income but not in publication losses, which Little, Brown shouldered during the formative years. The second and current contract is more equitable in that Little, Brown and The Society split profits equally. The expenses of the editorial office are now fully underwritten by our share of the profits.

Although Little, Brown and Company can trace its beginning to the year 1784 (which would make it almost as old as the United States), the company's official birthday is 1837, when Charles C. Little and James Brown, both in their thirties, put the assets of two predecessor companies into a partnership and gave it their names. Little, Brown has been a publisher of quality works since its inception, and The Society of Thoracic Surgeons is fortunate to have allied itself with a firm willing to do all possible to ensure success for *The Annals.* Authors such as Ralph Waldo Emerson, Henry Wadsworth Longfellow, Oliver Wendell Holmes, Daniel Webster, Samuel Eliot Morrison, Dumas Malone, James Hilton, Ogden Nash, J. D. Salinger, Herman Wouk, Norman Mailer, and Masters and Johnson are among the many who have been published by Little, Brown. John Steele and Herbert Sloan, Editors of *The Annals of Thoracic Surgery*, soon learned that they were in illustrious company.

The key people in our relations with Little, Brown are Mr. Fred Belliveau, Vice-President and General Manager of the Medical Division (Figs 8, 9), Mrs. Judith Kennedy, Administrative Manager of the Medical Division (Fig 9), and Mrs. Nancy Megley, Managing Editor for Medical Journals (Fig 10).

Conclusion

I feel deeply privileged to have been invited to join the small band of people who organized The Society of Thoracic Surgeons and to have served on the Council continuously in one role or another since the Founders Meeting in San Francisco in 1963. Serving as your President during the past year has been the greatest honor I have had in my life. Before stepping down, to be phased out after two more years on the Council as prescribed by the bylaws, I have one piece of advice for officers and councillors of the future: Remember, Smith, Bucklin and Associates are

Fig 9. Fred Belliveau with Judith Kennedy, Administrative Manager of Little, Brown's Medical Division, accepting subscriptions to The Annals of Thoracic Surgery *at the Twelfth Annual Meeting of our Society in Washington.*

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Fig 10. Nancy Megley, Managing Editor for Medical Journals at Little, Brown and Company.

professional multiple-association managers. Walter Purcell, Betty Perkins, and a host of supporting personnel are available to staff our current needs and any future programs we may develop. However, policies must be initiated and directed by the Council under the chairmanship of the President. If the Council fails in this responsibility, The Society will cruise at sea without a rudder and eventually will founder.

I am sure this will never happen. For as this overview has shown, The Society of Thoracic Surgeons is a well-organized and effective organization that has a dedicated technical staff to support the leadership of its officers, Council, and committees and that is well represented in the other key components of organized medicine. The challenges of the next decade will be continuing education, recertification, and manpower. We must prepare ourselves to face and deal with these issues, and we are well equipped to do so.

Author's Note

This presentation originally included 50 slides. Cost considerations made it necessary to reduce this number considerably for publication.

Open-Heart Experience in Infants Using Normothermia and Deep Hypothermia

Richard W. Pooley, M.D., Constance J. Hayes, M.D., Richard N. Edie, M.D.,
Welton M. Gersony, M.D., Frederick O. Bowman, Jr., M.D.,
and James R. Malm, M.D.

ABSTRACT **During the 9-year period from 1967 through 1975, 124 open-heart operations were performed on infants less than 1 year of age with 35 operative deaths (28%). Ninety-seven of these procedures used continuous cardiopulmonary bypass with normothermia or mild hypothermia, and 27 were done under deep hypothermia and circulatory arrest. Mortality and morbidity were similar regardless of the operative technique, although deep hypothermia facilitated the repair of complex lesions. The highest mortality occurred in infants less than 3 months of age. Respiratory insufficiency, usually requiring prolonged ventilatory support, occurred only among infants who had pulmonary overcirculation or congestion prior to operation. Adequacy of intraoperative repair and postoperative care were the major determinants of survival.**

With advanced technology and increasing experience, results of open-heart operations for infants with critical congenital heart disease have improved. Nevertheless, risk continues to be greater in this age group than in older children and adults [1].

Palliative operations have been helpful in the management of many infants with severe heart disease. However, this approach carries its own significant mortality and necessitates a subsequent corrective procedure, which becomes technically more difficult because of the first operation. Clearly, a single primary corrective procedure during infancy would be preferable if the mortality were less than the cumulative risk associated with palliation and later repair [2]. Experience with primary repair of severe defects in infancy has been increasing rapidly. Recently, several institutions have been carrying out open-heart correction using deep hypothermia with circulatory arrest because of the ease of repair afforded by the quiet heart and bloodless field [1, 4, 5, 18]. Other centers have developed expertise with continuous cardiopulmonary bypass and have been more selective in the use of deep hypothermia [2, 9, 16].

The infant open-heart experience at Columbia–Presbyterian Medical Center was reviewed in order to identify responsible factors in infant mortality and to compare the two operative techniques.

Material and Methods

During the 9-year period from 1967 through 1975, 124 open-heart operations (Table 1) were performed on infants who ranged in age from 2 days to 1 year. Eighty-four (68%) of the infants were less than 6 months of age, and, of these, 48 (39%) were under 3 months of age. The indications for operation were either severe hypoxia or congestive heart failure unresponsive to medical management. None of the procedures were elective. Sixty patients (48%) had cyanotic lesions. Eighty-nine (72%) of the patients had increased pulmonary blood flow, including 49 in the cyanotic group and 40 in the acyanotic group.

Continuous cardiopulmonary bypass with normothermia or mild hypothermia was used in 97 (78%) of these procedures. Cardiopulmonary bypass was carried out using a disposable Bentley bubble oxygenator with a blood prime including fresh acid-citrate-dextrose (ACD) or citrate-phosphate-dextrose (CPD) blood, calcium, TRIS buffer, and heparin [9]. In a few patients with high hematocrits, a clear or dilute blood prime was used. The average flow rate during total bypass was 150 ml/kg/min, and the

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From the Columbia University College of Physicians and Surgeons, New York, NY.

Presented at the Twelfth Annual Meeting of The Society of Thoracic Surgeons, Washington, DC, Jan 26–28, 1976.

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Table 1. Distribution by Lesion and Mortality of 124 Open-Heart Operations in Infants Less Than 1 Year of Age

Diagnosis	No. of Patients	Operative Deaths	Late Deaths
TAPVC	32	10	4
VSD	25	5	0
TGA	14	3	0
T/F	11	3	0
AS	11	2	1
ECD	5	2	1
Interr. arch	4	1	1
Miscellaneous	22	9	1
Total	124	35 (28%)	8

TAPVC = total anomalous pulmonary venous connection; VSD = ventricular septal defect; TGA = transposition of the great arteries; T/F = tetralogy of Fallot; AS = aortic stenosis; ECD = endocardial cushion defect; interr. arch = interrupted aortic arch.

average perfusion time was 61 minutes (range, 14 to 166 minutes).

Deep hypothermia with circulatory arrest was employed in the last 18 months with increasing frequency in selected cases (27 infants). This technique was carried out using surface cooling to approximately 25°C followed by core cooling with partial bypass to 15° to 20°C. Circulatory arrest time ranged from 27 to 88 minutes (average, 58 minutes). Following repair, the infants were rewarmed on partial cardiopulmonary bypass.

In order to assess the adequacy of oxygenation on total cardiopulmonary bypass, 13 determinations of oxygen consumption were made on 7 infants during their operations. Perfusion flow rates were taken from the calibrated flowmeter on the pump oxygenator. The LEX-O_2-CON* was used to measure oxygen content directly in arterial and mixed venous blood samples taken from the arterial and venous return lines of the perfusion system. All values were obtained after a stable flow rate had been present for at least 5 minutes. Oxygen consumption was determined as the product of flow rate and arteriovenous oxygen difference.

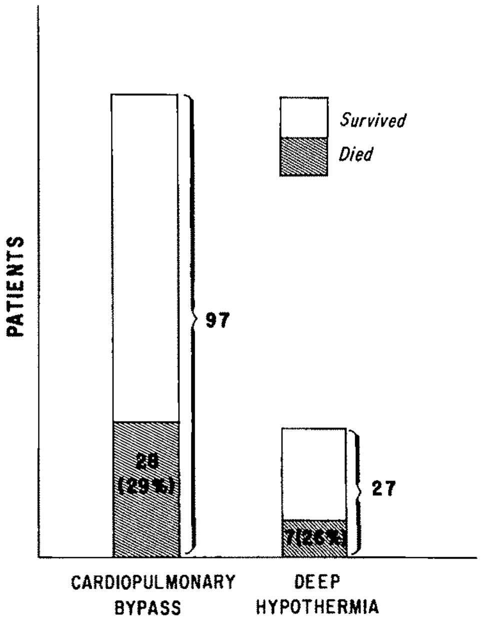
Results

Mortality

There were 35 operative deaths and 8 late deaths among the 124 procedures (see Table 1). Twenty-eight deaths (29%) occurred among the 97 patients operated upon under continuous cardiopulmonary bypass. Seven of the 27 infants (26%) undergoing operation with deep hypothermia died (Fig 1). Mortality was highest in the infants less than 3 months of age, and the survival rate improved with increasing age (Fig 2). The experience with individual lesions is illustrated in Figures 3 through 7. Of the 32 infants with total anomalous pulmonary venous connection (TAPVC), 22 were less than 3 months of age. Mortality in infants with this lesion was not related to age, but rather to the site of the abnormal venous connection (see Fig 3).

The operative deaths were divided into two major groups, as shown in Table 2. Those deaths which occurred despite what appeared to be adequate intraoperative repair and postoperative management were categorized as probably unavoidable. There were 9 patients in this group. Four died as a result of unexplained low cardiac output. All had membranous ventricular septal defects, 3 with major associated lesions.

Fig 1. Comparison of operative mortality in 124 infant open-heart operations using continuous cardiopulmonary bypass and deep hypothermia.



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*Lexington Instruments Corp, Waltham, MA.

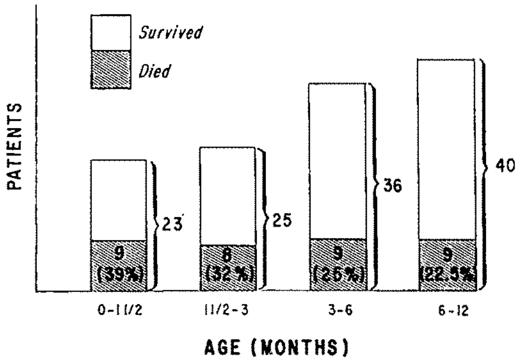

Fig 2. Operative mortality in 124 infant open-heart operations as related to age.

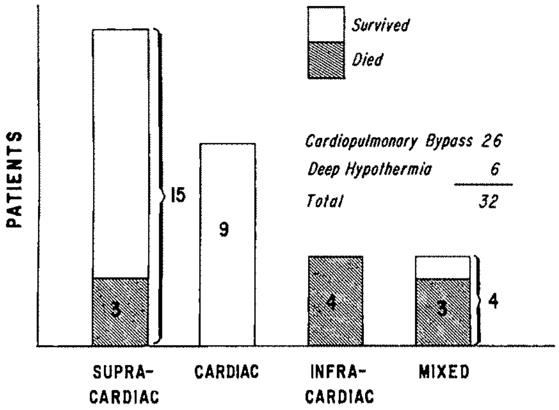

Fig 3. Operative mortality in infant open-heart operations for total anomalous pulmonary venous connection according to site of connection.

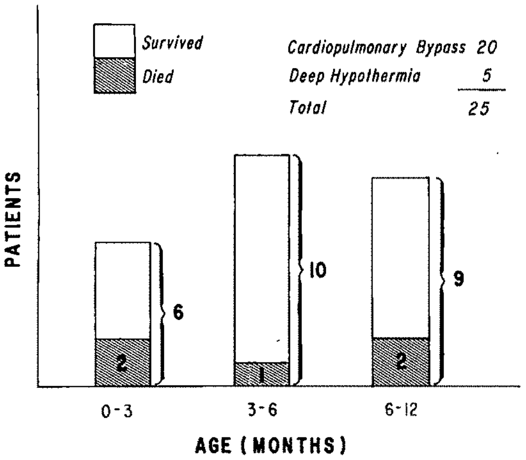

Fig 4. Operative mortality in infant open-heart operations for ventricular septal defect according to age.

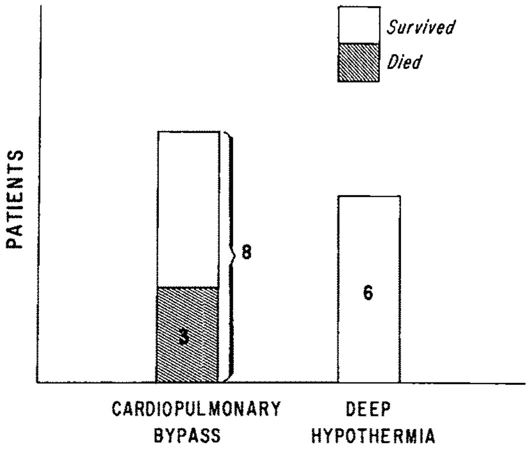

Fig 5. Comparison of infant operative mortality following Mustard procedure for transposition of the great arteries using continuous cardiopulmonary bypass or deep hypothermia.

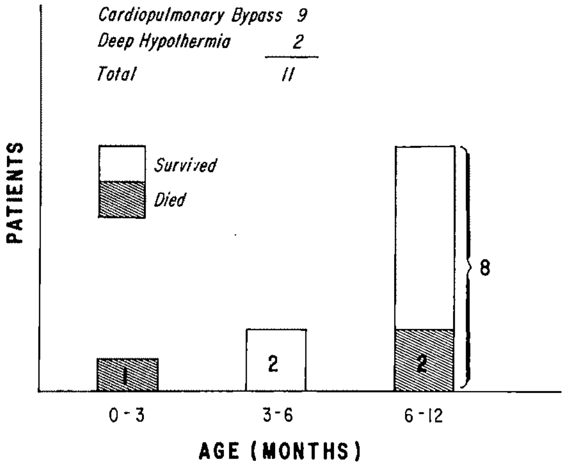

Fig 6. Operative mortality in infant open-heart operations for tetralogy of Fallot according to age.

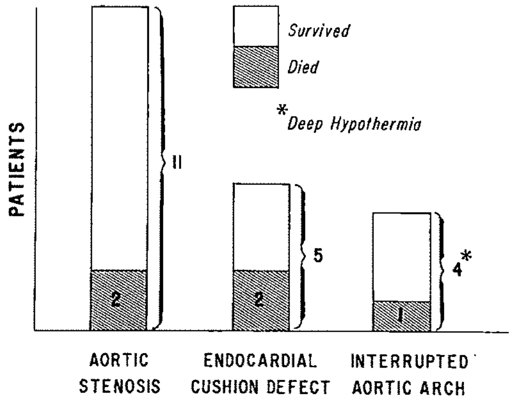

Fig 7. Operative mortality in infant open-heart operations for aortic stenosis, endocardial cushion defect, and interrupted aortic arch.

Table 2. Factors Responsible for 35 Deaths in 124 Open-Heart Operations in Infants Less Than 1 Year of Age

Factors in Death	No. of Deaths[a]	Percent
Probably unavoidable		
Unexplained low cardiac output	4	
Primary myocardial failure	3 (2)	
Obstructive pulmonary vascular disease	2 (1)	
Total	9	26
Potentially avoidable		
Intraoperative		
Incomplete repair	8 (1)	
Bleeding	5 (1)	
Diagnostic error	2 (1)	
Inadequate bypass	1	
Total	16	46
Postoperative		
Inadequate ventilatory management	4	
Inappropriate blood volume replacement	3	
Cardiac tamponade	1	
Hyperkalemia	1	
Arrhythmia	1 (1)	
Total	10	28

[a] Numbers in parentheses represent patients operated upon under deep hypothermia.

Three patients had primary myocardial failure and could not be weaned from bypass due to inadequate left ventricular function. Obstructive pulmonary vascular disease was present in 2 infants who died intraoperatively.

In retrospect the remaining deaths might have been avoided, and the responsible factors were separated into intraoperative and postoperative categories. Sixteen infants died of complications that occurred during the operation. Eight of these had incomplete repair, of whom 4 had TAPVC. Intraoperative bleeding was responsible for the death of 5 infants. Diagnostic errors led to inappropriate operative management in 2 patients. In 1 of these, strong angiographic evidence of a muscular ventricular septal defect (VSD) led to an unnecessary left ventriculotomy. A subsequent right ventriculotomy was required to close the membranous defect. An unrecognized patent ductus arteriosus in an infant with transposition of the great arteries (TGA) and VSD accounted for the other death. Technical difficulties with bypass resulted in poor perfusion, severe acidosis, and death in another infant. Inadequate ventilatory support, inappropriate blood volume replacement, cardiac tamponade, hyperkalemia, and sudden heart block were the precipitating events among the infants who died after operation.

Morbidity

Morbidity associated with the techniques of continuous cardiopulmonary bypass and deep hypothermia was evaluated in terms of ventilator time, intensive care unit (ICU) time, and postoperative hospitalization (Fig 8). The mean ventilator time was 2 days for the group operated upon under continuous bypass and 3.4 days for the deep hypothermia group. Mean ICU time was 4.7 and 6.3 days, respectively. There was no significant difference in the postoperative hospitalization time of the two groups; this averaged 20 days in the continuous bypass

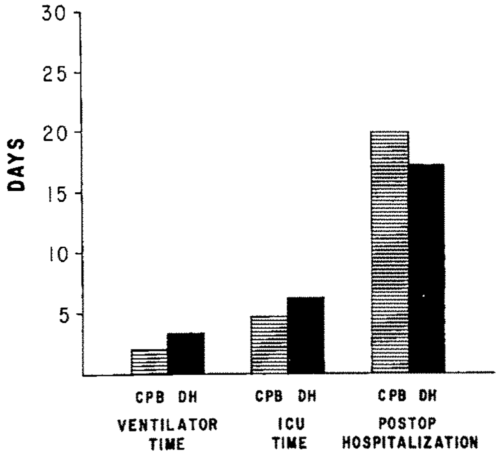

Fig 8. Morbidity in infant open-heart operations in terms of ventilator time, intensive care unit (ICU) *time, and postoperative hospitalization: comparison of continuous cardiopulmonary bypass* (CPB) *and deep hypothermia* (DH).

group and 17 days in the deep hypothermia group.

The specific complications encountered are listed in Table 3. Twenty-three infants had significantly low cardiac output necessitating prolonged support with one or more inotropic agents; 21 of these patients died. Life-threatening arrhythmias occurred in 6 infants, and 2 infants had cardiac tamponade. Persistent significant pulmonary problems, usually requiring ventilatory support in excess of 4 days, occurred in 18 patients, all of whom had preoperative pulmonary overcirculation or congestion. Half of these patients had a clinical history of respiratory disease prior to operation. Upper airway obstruction was significant in 3 patients, 1 of whom required tracheostomy. Definite seizures occurred in 6 patients; 5 of these had associated metabolic or hematological abnormalities such as hypoglycemia, hypocalcemia, hyponatremia, or disseminated intravascular coagulation. Intrinsic renal failure was seen only as a manifestation of severe low cardiac output and was a poor prognostic sign.

Oxygen Consumption

The 13 determinations of oxygen consumption made in 7 infants while on total cardiopulmonary bypass fell within the expected range for infants under general anesthesia without bypass, as shown in Figure 9 [10–12, 15, 17]. These data suggest that the oxygen requirements of the continuous bypass group were satisfied at the perfusion flow rates attained.

Comment

The overall mortality in this series was highest in those infants less than 3 months of age. This finding is in agreement with reports of Sade and associates [14] and Bonchek and co-workers [2], who also found mortality inversely related to age. In addition, the specific cardiac defect was an important factor in the outcome, as illustrated by the mortality in TAPVC (see Table 1, Fig 3). Barratt-Boyes and his co-workers [1] and Rittenhouse and colleagues [13] also found that

Table 3. Postoperative Complications Following 124 Open-Heart Operations in Infants Less Than 1 Year of Age

Complication	No. of Patients[a]	Comment
Cardiac		Incidence 25%
Low-output syndrome	23 (2)	24 additional patients required transient inotropic support
Arrhythmias	6 (2)	13 additional patients displayed mild temporary rhythm abnormalities
Tamponade	2 (1)	
Respiratory		Incidence 17%
Respiratory insufficiency	18 (6)	All had preoperative pulmonary overcirculation or congestion
Upper airway obstruction	3 (2)	
Central nervous system		Incidence 5%
Seizures	6 (2)	5 had recognized metabolic or hematological abnormalities

[a] Numbers in parentheses represent patients operated upon under deep hypothermia.

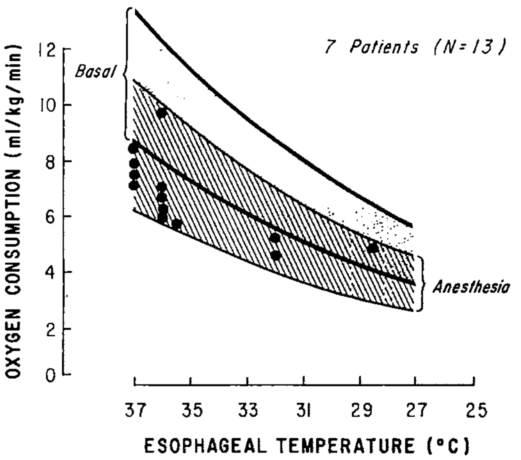

Fig 9. Oxygen consumption in 7 infants on total cardiopulmonary bypass.

mortality varies according to the specific cardiac lesion.

Survival did not appear to be influenced by the operative technique employed; however, the quiet heart and bloodless field afforded by deep hypothermia have been extremely helpful in the repair of complex defects such as interrupted aortic arch and TAPVC. On the other hand, when a short operative procedure is anticipated, as in aortic stenosis, or if intracardiac mapping is to be carried out, continuous cardiopulmonary bypass remains the technique of choice at this institution.

Morbidity was not related to the operative technique. Although ventilator time and ICU time were slightly increased in the deep hypothermia group, this probably reflects a recent change in ventilator management. There has been a greater use of intermittent mandatory ventilation during the last 18-month period, when deep hypothermia began to be used with increasing frequency. With this system, the infants are permitted to breathe spontaneously between intermittent mechanical ventilations, allowing a gradual and more physiological return to normal breathing [6]. However, the patients remain intubated somewhat longer.

Of the specific postoperative problems encountered, only cardiac complications carried a grave prognosis. The mortality associated with low cardiac output was especially high, and this problem always suggests the possibility of an incomplete cardiac repair. In many instances, however, the etiology of the low-cardiac-output syndrome cannot be documented.

Respiratory complications were related to preoperative pulmonary overcirculation, although half of these patients had no clinical history of pulmonary problems prior to operation. Abnormalities in lung function in overperfused infant lungs have been reported in the absence of clinical respiratory disease [8]. It was a striking observation that among the infants with normal or low pulmonary artery pressure prior to operation, serious postoperative pulmonary complications did not occur. Barratt-Boyes and associates [1] have reported a virtual absence of postoperative pulmonary complications when deep hypothermia is employed. In this series, use of the deep hypothermia technique did not significantly lower the incidence of pulmonary complications as compared with the continuous bypass method; however, no infant died of progressive pulmonary insufficiency.

There was no clinical evidence of intraoperative hypoxia, regardless of operative technique. Furthermore, adequate oxygen consumption was documented in the continuous cardiopulmonary bypass group (see Fig 9). Seizures were uncommon and appeared to be related to metabolic or hematological abnormalities rather than the operative technique. This contrasts with other reports [3, 18] in which seizures were thought to be related to the deep hypothermia method. In this series, no patient sustained a permanent neurological deficit.

Renal failure was observed only in association with severe low cardiac output and did not occur selectively among infants who were operated upon during deep hypothermia. This differs from the experience of Venugopal and associates [18], who thought that the deep hypothermia technique was an etiological factor in renal failure in some instances.

The most important determinants of survival after open-heart operation in infancy were the adequacy of intracardiac repair and postoperative management. The prospects for successful operative management have improved markedly over the past 5 years; however, even better results are possible. In retrospect, 75% of the infant deaths in this series were related to potentially avoidable factors, two-thirds of which occurred intraoperatively. This underscores the critical need for carefully planned, meticulous operative technique and postoperative care in the management of these severely ill infants [7].

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Discussion

DR. BRUCE J. INNES (Norfolk, VA): I congratulate the authors on their excellent presentation and on the obviously great attention paid to detail in their studies over the last 9 years. I think the fact that none of these patients had elective operation reflects the severity of problems in these very sick infants.

I would be interested to know if the authors had done a biochemical analysis of the blood prime before or during bypass. On several occasions we have observed very high potassium levels in the prime before bypass was instituted that may have been the cause of some subsequent problems.

I also would be interested in knowing more about the inotropic agents they used and about monitoring in the postoperative period. Were left atrial lines or other pressure-monitoring devices used, and was cardiac output measured frequently in those patients who began to manifest the signs of low cardiac output?

DR. EDUARDO ARCINIEGAS (Detroit, MI): At Children's Hospital in Detroit we use deep hypothermia and circulatory arrest only for lesions, such as total anomalous pulmonary venous return and transposition of the great arteries, in which having a bloodless, quiet field is essential for accurate and speedy repair. Most other lesions can be handled adequately with high-flow normothermic perfusion.

Our experience over the past 4 years includes 60 patients under 1 year of age with an overall mortality of 26%. Closure of ventricular septal defect was done in 9 patients with 1 death. High-flow normothermic perfusion was used in these and in 13 patients with aortic valvotomy, among whom there were 4 deaths that were largely related to endocardial fibroelastosis and annular hypoplasia. Hypothermic circulatory arrest was particularly useful in the repair of total anomalous pulmonary venous return, in which 4 deaths among 8 patients were partly attributable to late diagnosis and high pulmonary vascular resistance. In simple transposition of the great arteries, circulatory arrest was used in a limited fashion (14 patients, 1 death). The miscellaneous group (16 patients, 6 deaths) includes complete atrioventricular canal, complicated transposition, and other complex lesions for which normothermia or hypothermia was used selectively.

We believe that hypothermic arrest is an excellent tool but that it should be used selectively, in relation to the type of lesion, rather than merely on the basis of the patient's size or weight.

DR. JAROSLAV STARK (London, England): Our experience with open-heart operations in the first year of life is very similar to that presented by Dr. Malm's group. Between May, 1971, and December, 1975, we operated on 196 infants. Of those treated during the first 3 months of life, 55 (83%) were operated upon under deep hypothermia and circulatory arrest and 11 (17%) under conventional bypass in which moderate hypothermia was used. In patients between 3 and 6 months of age, both methods were used about equally; over the age of 6 months, 73 (92%) were operated upon using cardiopulmonary bypass. The results depend to a great extent on the basic lesion and its severity. In our series the hospital mortality rate was low for patients with uncomplicated transposition of the great arteries (6%, 3 of 52 operated infants) and ventricular septal defect (3%, 1 of 34 patients). It was higher in patients with complex transposition (28%, 4 of 14 operations) and total anomalous pulmonary venous drainage (36%, 14 of 39 patients).

With regard to technique, I would like to mention a combined bypass and hypothermia method that we use frequently in infants with complex lesions such as truncus arteriosus. Operation is started under circulatory arrest in deep hypothermia. The pulmonary artery is detached from the truncus, the defect in the aorta is closed, anastomosis between the conduit and the pulmonary artery is performed, and the ventricular septal defect is closed. When we think the time limit of 60 minutes may be exceeded, the two caval cannulas are inserted through the opened right atrium and operation is completed on bypass while the patient is being rewarmed. We do not have to work under the pressure of a 60-minute time limit, and yet we derive the benefit of a bloodless field during the difficult part of the procedure.

DR. S. SUBRAMANIAN (Buffalo, NY): I think one of the things we fail to recognize is that the results obtained with either hypothermia or cardiopulmonary bypass are related to the infant's symptoms. The infant who comes to operation on an emergency basis following failure of medical treatment carries a much higher risk of death than an infant in whom the operation is done as a semielective procedure.

We decided to look at our data based on the symptoms of the infants in our series. As shown in the Table, there are four groups of patients: Group I consists of patients who were emergencies, representing a failure of medical treatment. Group II had elective operations in which primary correction was offered to the child in view of the unfavorable natural history of the disease, such as occurs in transposition, which carries a high incidence of pulmonary vascular disease. Group III patients were those in whom an emergency operation was done following failure of palliative operation, and Group IV had elective procedures in which initial palliation was followed by early corrective operation, such as for transposition with ventricular septal defect.

If you analyze this information, the highest mortality was obtained, naturally, in the group of infants in whom operation was done as an emergency procedure. On the other hand, mortality was almost zero for patients with simple transposition of the great arteries, complex transposition, ventricular septal defect, and other infants for whom operation was suggested in the first year of life to prevent complications associated with the natural history of the disease (such as pulmonary vascular disease, which could preclude corrective operation). Similarly, for elective

Types of Operations in 4 Groups of Infants with Congenital Heart Lesions

	Reason for Operation[a]			
	Group I[b]	Group II[c]	Group III[d]	Group IV[e]
TGA—simple	14 (4)	22 (0)	...	...
TGA—complex	20 (10)	8 (0)	...	7 (0)
VSD	18 (1)	3 (0)	4 (0)	...
TAPVC	11 (5)	...	...	...
T/F	12 (2)	...	2 (2)	...
Miscellaneous	22 (9)	1 (0)	...	...
Total	97 (31)	34 (0)	6 (2)	7 (0)

[a] Numbers in parentheses represent deaths.

[b] Emergency—failure of medical treatment.

[c] Elective—primary correction.

[d] Emergency—failure of palliation.

[e] Elective—after palliation.

operation following palliation at an early age, as in patients with transposition and ventricular septal defect who had undergone early banding, the mortality again was negligible.

So I think it is important that we look at these infants individually, not as a total group; otherwise it is like comparing apples, bananas, and oranges. You can take a 2-month-old patient with transposition, perform a semielective operation, and have a zero mortality. On the other hand, a 2-month-old patient with a simple ventricular defect who is extremely moribund can die after operation.

DR. POOLEY: In answer to Dr. Innes's questions, we have measured cardiac output in approximately one-third of these infants, and in general they correlate poorly with the blood pressure. The second thing that we have noted is that the outputs are significantly lower in infants—even infants who are doing well—than in children over 1 year of age. In addition, we have noted that a lack of response to isoproterenol is a poor prognostic sign.

For monitoring we routinely use an arterial line and a right atrial line, and in selected patients we use a left atrial line. The inotropic drug that we routinely used in the past was isoproterenol. More recently dopamine has been employed and has been found useful in selected patients. Interestingly, some patients who do not respond well to isoproterenol may improve with dopamine or a combination of the two drugs.

Our present policy is to use deep hypothermia for complex cardiac lesions despite the fact that our mortality figures do not indicate a difference between the two techniques. The deep hypothermia group is too small to allow us to draw any strong conclusions with regard to mortality at this time. However, we are hopeful that this technique will result in improved long-term survival in patients with complex congenital lesions such as total anomalous veins, transposition, or interrupted aortic arch. We are less optimistic about the influence of deep hypothermia on postoperative course, complications, and morbidity, which we believe are related to factors other than the operative technique.

Effect of Hypothermic Anoxic Cardioplegia on Myocardial Contractility

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Richard A. Shinto, B.A., and John E. Connolly, M.D.

ABSTRACT **A study was undertaken to ascertain the protective effect of topical hypothermia on the anoxic heart. The presence or absence of myocardial damage was judged by myocardial contractility. The papillary muscle of an excised rabbit heart was detached from the mitral annulus and interposed between a fixed point and a force/displacement transducer. The maximal net developed tension (T_{Nmax}) of the papillary muscle with normothermic coronary perfusion was used as an index of myocardial contractility. With each temperature drop of 10°C, the anoxia time that resulted in the same recovery level of T_{Nmax} was prolonged by a factor of 2.8. A nomogram was constructed correlating percent of myocardial recovery seen with different degrees of myocardial hypothermia during various anoxic periods. Optimum protection was noted at a myocardial temperature of 18°C.**

Although anoxic cardioplegia provides a quiet, dry operative field, it is occasionally associated with irreversible myocardial damage. In 1957 Cross and associates [3] introduced the technique of topical cooling in order to protect the heart from anoxic damage. They perfused the aortic root with cold (0°C) blood after the ascending aorta was cross-clamped. Shumway and Lower [12] found that effective myocardial cooling could be achieved by pericardial lavage with cold (4°C) normal saline. Urschel and Greenberg [15] modified the Cross technique by adding perfusion of the aortic root with cold (1°C) lactated Ringer's solution to cold pericardial lavage. Although topical hypothermia has been widely employed clinically, there are few studies [1, 4] in which subsequent cardiac function has been used to assess the protective effects of hypothermia. In addition, none of these experimental studies has provided guidelines to indicate what myocardial temperatures are required for various periods of anoxia; therefore, the present study was undertaken to answer these questions. Presence or absence of myocardial damage was ascertained by studying myocardial contractility in a papillary muscle of the rabbit heart. This information then permitted the construction of a nomogram correlating percent of myocardial recovery seen with different degrees of myocardial hypothermia during various anoxic periods.

Methods

New Zealand white rabbits weighing 2.1 to 2.8 kg were anesthetized with intravenous sodium pentobarbital (25 mg/kg) supplemented with intramuscular ketamine hydrochloride, 5 mg/kg. After the animal was intubated and placed on a mechanical respirator, complete muscle relaxation was obtained by intravenous administration of succinylcholine chloride (2 mg) and *d*-tubocurarine chloride (0.5 mg). The chest was opened through a midsternum incision, the animal was heparinized (5 mg/kg), and approximately 70 ml of blood was aspirated from the right atrium and used to prime a circuit consisting of a miniature pump-oxygenator, a heat exchanger, an overflow reservoir, a filter, and a roller pump (Fig 1). The ascending aorta was cannulated and perfused retrograde with lactated Ringer's solution at 18°C and at 100 cm H_2O. The heart was quickly excised and immersed in cold saline (18°C). Through a wide left atriotomy one leaflet of the mitral valve was incised and the tip of the posterior papillary muscle was detached from the annulus by dividing

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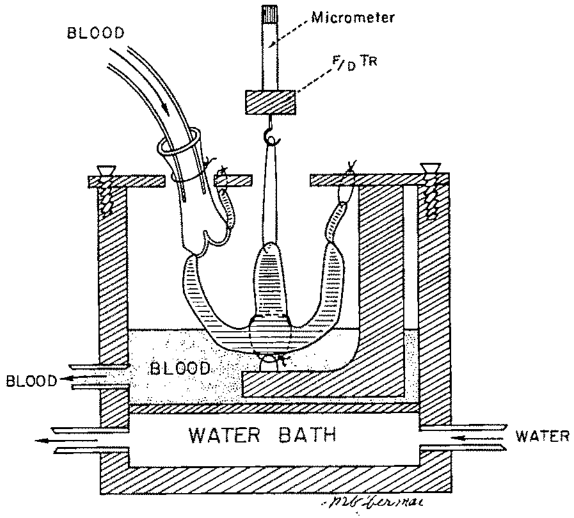

Fig 1. The rabbit heart preparation. Coronary perfusion is provided by a retrograde aortic cannula. The papillary muscle is interposed between a fixed point and a force/displacement transducer (F/$_D$ Tr) *which is mounted on a micrometer after the mitral valve has been excised.*

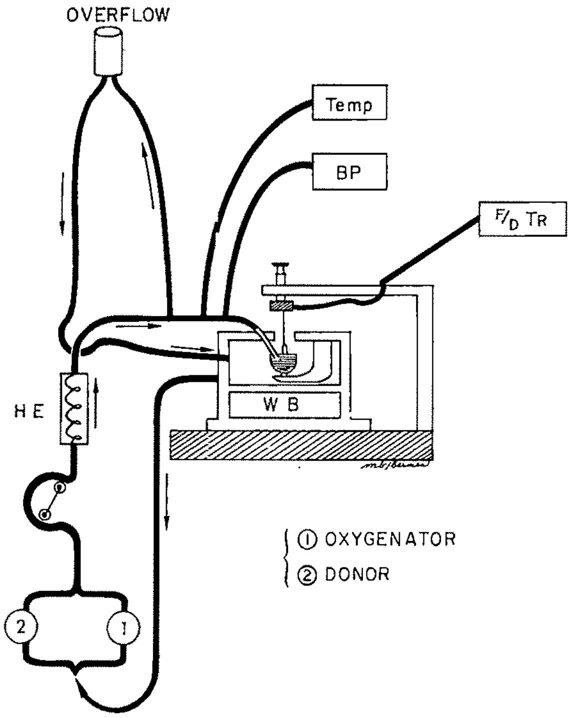

Fig 2. The experimental circuit. (BP = *strain gauge transducer for blood pressure;* F/$_D$ Tr = *force/displacement transducer;* HE = *heat exchanger;* Temp = *thermistor probe for temperature monitoring;* WB = *water bath.)*

the chordae tendineae. The posterior papillary muscle was then suspended between a fixed point and a force/displacement transducer (Fig 2). Following these preparations, coronary perfusion was begun at a pressure of 80 mm Hg and a temperature of 37°C.

Myocardial temperature was continuously measured by a needle thermistor. Arterial Po_2, Pco_2, and pH were checked at intervals using a blood gas analyzer. Arterial Po_2, Pco_2, and pH were maintained within normal limits by adjusting the gas flow (O_2, CO_2, and N_2) of the oxygenator and by administering a 7.5% sodium bicarbonate solution. The spontaneous heart rate with this preparation averaged 230 beats per minute. A length/tension curve of the papillary muscle was then obtained as follows. The papillary muscle tension at rest (T_R) and the total developed tension (T_T) were continuously recorded. The net developed tension (T_N) was defined as $T_N = T_T - T_R$. The papillary muscle length at which T_R started to rise from zero when the papillary muscle was gradually stretched was defined as zero length. The papillary muscle was stretched in increments of 0.5 mm every 10 seconds until T_N reached its maximum, which was called T_{Nmax}. This length/tension curve was obtained every 10 minutes until T_{Nmax} became stabilized (baseline T_{Nmax}).

After baseline values had been established, the experiments were divided into two groups. In a control group of 10 experiments the length/tension measurements were repeated every 10 minutes for an additional period of 90 minutes without interrupting coronary perfusion. In a second group of 70 experiments, coronary perfusion was stopped and the heart was immersed in normal saline solution of varying temperatures while anoxia time was varied from 15 minutes to 10 hours (Fig 3). After each anoxic period the heart was reperfused with oxygenated blood at 80 mm Hg and 37°C until papillary muscle contractility fully recovered. The T_{Nmax} at this point was expressed as a percentage of baseline and was referred to as percent recovery.

Results

As soon as the excised hearts were perfused with oxygenated blood, their papillary muscles started to contract in normal sinus rhythm and T_{Nmax} continued to increase. Approximately 1 hour was required before T_{Nmax} reached a plateau (baseline T_{Nmax}).

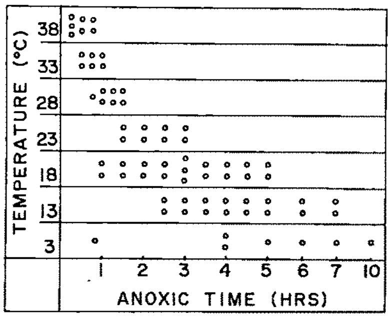

Fig 3. Diagram plotting 70 experiments varying the myocardial temperature during anoxia and the duration of anoxia. Each open circle represents a separate experiment.

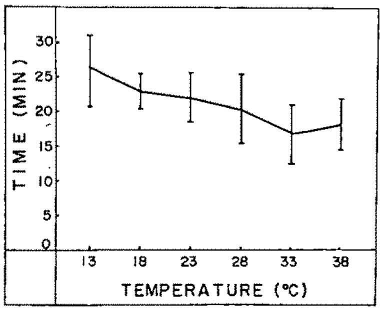

Fig 5. The correlation between the time required for recovery of contractility and the myocardial temperature during anoxic cardioplegia is shown. Bars signify standard deviations. The lower the myocardial temperature, the longer the time required for recovery of contractility.

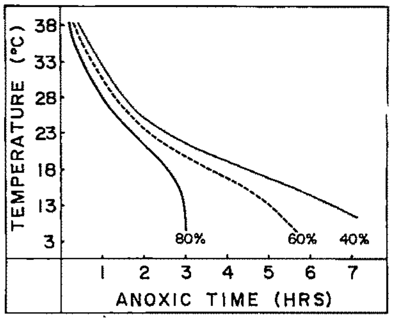

Fig 4. Nomogram expressing anoxia time, myocardial temperatures, and percentage recovery of papillary muscle contractility after reperfusion. Solid line *signifies 80 % recovery of T_{Nmax},* broken line *60 %, and* dashed line *40 %.*

In the control group T_{Nmax} fell to 97 ± 2% (mean ± standard deviation) of baseline values at the conclusion of 2½ hours of uninterrupted coronary perfusion. In the experimental group with anoxic cardioplegia, the myocardial temperature rapidly equilibrated with the temperature of the cold saline in which the heart was immersed. After reperfusion, ventricular fibrillation occurred but spontaneously converted to sinus rhythm within 15 minutes.

The T_{Nmax} gradually increased after reperfusion over periods of 50 to 70 minutes. The percent recovery of T_{Nmax} in each experiment was plotted on a graph expressing myocardial temperature during anoxia and the length of anoxia time. Then 80%, 60%, and 40% recoveries were estimated to construct a nomogram as shown in Figure 4. The percent recovery of T_{Nmax} after a given duration of anoxia was significantly augmented by hypothermia, as shown in this nomogram. With each temperature drop of 10°C, the anoxia time that resulted in the same recovery level was prolonged by a factor of 2.8 ± 0.3. Figure 5 shows the correlation between myocardial temperature and the time required for recovery of papillary muscle contraction after reperfusion. As noted, the lower the myocardial temperature, the longer the perfusion time required for recovery.

Comment

The effects of hypothermic anoxic cardioplegia on left ventricular function after reperfusion have been studied by others [1, 4, 12] using an in situ canine heart while the animal was supported by total cardiopulmonary bypass. In these studies a correlation between left atrial pressure and cardiac output was determined or the isovolumetric contractility of the left ventricle was studied using a latex balloon placed inside the left ventricle. Both methods were noted to be technically complicated and associated with many variables that were often difficult to control. An alternative to measuring left ventricular function after reperfusion is to measure the myocardial contractility by a Walton-Brodie strain gauge or an impedance plethysmographic capillary sutured to the left ventricular wall. The disadvantages of these methods are the difficulty in placing a strain gauge or capillary precisely in the direction of the contracting myocardial fibers and the problems in adjusting the zero point of a transducer to measure resting myocardial tension.

A papillary muscle preparation [2, 13] has been widely employed to study the mechanics of myocardial contraction. A thin papillary muscle is excised and immersed in cold balanced salt solution which is saturated with oxygen. The isometric contractility of the electrically stimulated papillary muscle is then measured. Technically, this preparation is simple and more reproducible than other methods used for left ventricular function studies. However, such an excised papillary muscle preparation could not be used in this study because normothermic coronary perfusion is required before and after hypothermic anoxic cardioplegia.

The experimental model described here has a unique feature, namely, that papillary muscle contractility can be accurately measured while coronary perfusion is precisely regulated. Our control studies demonstrated the stability of papillary muscle contractility over 2½ hours with this technique.

Our study showed the significant protective effects of hypothermia on the anoxic heart. Greenberg and co-workers [4] studied the correlation between myocardial temperature and left ventricular function after anoxic cardioplegia in dogs. These investigators found that mild depression of left ventricular function occurred after anoxia periods of 10 minutes at 37°C, 15 minutes at 28°C, 30 minutes at 18°C, and 60 minutes below 10°C; moderate depression occurred after 15 minutes at 37°C, 20 minutes at 28°C, and 45 minutes at 18°C; and severe depression occurred after 30 minutes at 37°C and 30 minutes at 28°C. Angell and associates [1] also studied the maximum tolerable length of anoxia in the canine heart. They estimated the viability of the heart from the heart rate, presence of rhythm disturbance, weight gain, gross and microscopical appearance of the heart, left ventricular contractility as measured by a latex balloon technique, coronary sinus blood enzymes, and subsequent orthotopic transplantation into recipient dogs. They concluded that the maximum allowable anoxia intervals were 35 minutes at 37°C, 115 minutes at 24°C, and 230 minutes at 15°C. When the duration of anoxia and myocardial temperature in Angell's experiments are plotted on our nomogram, their maximal allowable intervals are found to match the 60% recovery curve. Using experiments similar to those of Greenberg and colleagues [4], Mundth and his associates [8] reported that 60 minutes of anoxia at 28°C resulted in 75% recovery of left ventricular function. When Mundth's variables are plotted on our nomogram, the predicted percent recovery is 80%. It is of interest to note that the results obtained with both left ventricular function and papillary muscle preparation techniques closely approximate one another, even in different species. Tsifutis and associates [14] compared myocardial contractility in rats and human beings and found little difference between the two. This would support our contention that a nomogram constructed from rabbit heart experiments can be applied to humans.

The safe period of anoxia for human hearts has been reported by several investigators [5–7, 9] to vary between 60 and 128 minutes using hypothermic cold lavage. Sanger and co-workers [11] reported that 120 minutes of anoxic cardioplegia with ice saline slush was tolerated in humans. Subsequently the same group [10] revised their recommendation and advised that anoxia periods should be limited to 50 to 60 minutes during topical hypothermia. From our nomogram it can be seen that the maximal tolerable anoxia period can be prolonged nine times by cooling the heart to 18°C. However, if the temperature is reduced below 18°C, this protective effect of hypothermia becomes progressively less; in addition, longer periods are required for recovery of myocardial contractility following extreme hypothermia. Functional recovery of hearts subjected to such profound hypothermia requires in turn prolongation of cardiopulmonary bypass to allow myocardial recovery.

In conclusion, topical hypothermia is a safe, effective method of protecting the anoxic heart. Monitoring of myocardial temperature by a thermistor needle and the use of our nomogram should permit maximum protection against anoxic injury when employing topical hypothermia. The optimal beneficial effect of hypothermia occurs at a muscle temperature of 18°C. Myocardial temperatures below 18°C confer little additional protection and at the same time prolong bypass.

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Effects of Morphine and Halothane Anesthesia on Coronary Blood Flow

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ABSTRACT **This study was undertaken to determine the relative effects of morphine and halothane anesthesia on coronary blood flow. Right heart bypass was instituted in 20 dogs by draining the vena cava blood into a cardiotomy reservoir and returning it to the main pulmonary artery. Coronary sinus drainage was measured by a right ventricular cannula. Group I (10 dogs) was sequentially given 0.5, 1, 1.5, 2.0, and 2.5% halothane. Group II (10 dogs) was given 1, 2, 3, 4, and 5 mg per kilogram of morphine intravenously. Arterial pressure, coronary sinus blood flow, cardiac output, arterial pH, P_{CO_2}, and P_{O_2} were determined and repeated at each dose level of anesthesia and compared to the control values.**

Morphine significantly increased coronary flow at 3, 4, and 5 mg/kg without pressure adjustment and at 2 mg/kg after pressure adjustment. Coronary flow with halothane was unchanged from control values except for a decrease at 2.5%. Coronary flow was significantly greater with 3, 4, and 5 mg/kg of morphine than with 1.0 and 1.5% halothane.

Morphine and halothane are among the most common anesthetic agents used for patients undergoing heart operations. However, halothane has been shown to decrease myocardial contractility, left ventricular work, and myocardial oxygen utilization [5, 9, 10, 11]. Myocardial blood flow has been found to decrease during halothane anesthesia in a dose-dependent fashion occurring in proportion to the myocardial depression [6, 11, 13]. In contrast, the hemodynamic effects of morphine in the cardiac patient have been favorable; they include improvement in the cardiac index and stroke index and decreased systemic vascular resistance [1, 3]. Studies on the effects of morphine on coronary blood flow are sparse, and the reported findings vary considerably [4, 8].

The following study was undertaken as an initial step in an effort to determine the relative effects of morphine and halothane anesthesia on coronary blood flow, independent of cardiac output or aortic pressure.

Clinical Material and Methods

Twenty conditioned adult mongrel dogs were given an initial intravenous dose of sodium thiopental, intubated, and had catheters inserted into the aortic root by way of the femoral artery and into the superior vena cava through the left external jugular vein. A bilateral thoracotomy was performed, the azygos vein was ligated, and the venae cavae and main pulmonary artery were encircled with umbilical tapes. Cannulas were inserted into the superior and inferior venae cavae through the right external jugular and femoral veins, respectively, and into the main pulmonary artery. The caval cannulas were connected to a Bentley pediatric oxygenator, and the pulmonary artery cannula was used for return flow from the pump. The system was primed with Ringer's lactate solution, right heart bypass was instituted (Fig 1), both caval tapes were tightened, and a right ventricular sump catheter was inserted and connected for gravity drainage into the venous circuit. The pulmonary artery tape was then tightened, thus excluding the right atrium and ventricle from the circulation. Venous drainage from the animal was returned by a roller pump to the pulmonary artery distal to the tape, and once the circulation was stabilized, the same pump flow was maintained for the remainder of the experiment.

Baseline measurements were then recorded. These included heart rate, arterial and central

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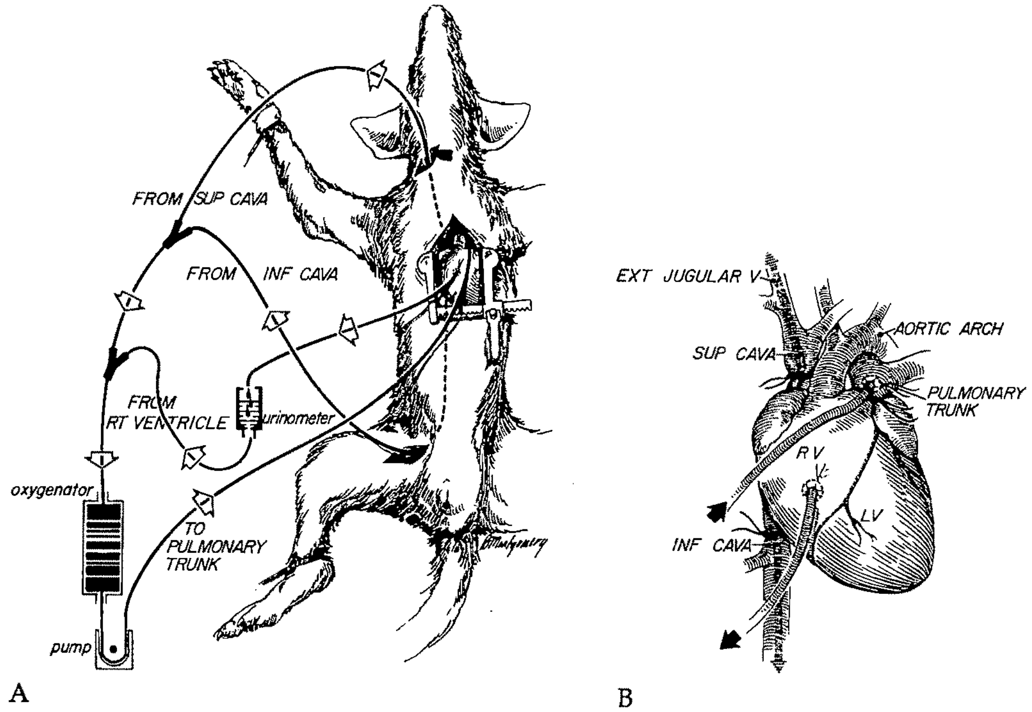

Fig 1. Right heart bypass. The right atrium and ventricle drain separately into the venous circuit by way of the right ventricular catheter, allowing measurement of coronary sinus flow with return of blood into the main pulmonary artery. (RV = *right ventricle;* LV = *left ventricle.)*

venous pressures, cardiac output (pump return), arterial pH, P_{CO_2}, P_{O_2}, and coronary sinus return (right ventricular sump catheter).

The animals were divided into two groups of 10 each. Group I received inhaled concentrations of 0.5, 1.0, 2.0, and 2.5% halothane. Group II received increasing intravenous doses of 1, 2, 3, 4, and 5 mg/kg of morphine sulfate. The animals in both groups were allowed to stabilize for 15 minutes following each dose change, and the baseline studies were repeated. When mean arterial pressure decreased, restoration of aortic root pressure to control values was attempted by increasing the peripheral resistance. This was done by tightening a constricting tape around the descending aorta. Another set of values was then obtained.

At the termination of the experiment the hearts were removed and weighed.

Results

HEART RATE. The average baseline rate in the halothane group was 101 beats per minute, and the rate progressively decreased to 81 following inhalation of the 2.5% concentration of halothane. The heart rate in the morphine group also demonstrated a reduction, beginning at 95 and decreasing to 81 after 5 mg/kg of morphine had been administered.

CARDIAC OUTPUT. The cardiac outputs were maintained at a constant level by the pump inflow, and, as noted in Figure 2, they ranged from 35 to 40 ml/kg/min throughout the procedure.

MEAN ARTERIAL BLOOD PRESSURE. The halothane group showed a progressive decrease from a mean arterial pressure of 61 to 33 mm Hg at the 2.5% concentration level (Fig 3). The initial average arterial pressure in the morphine group was 44 mm Hg, decreasing to 36 mm Hg after 1 and 2 mg/kg of morphine, increasing to 59 mm Hg after 3 mg/kg of morphine, and then remaining at 41 mm Hg for the duration of the experiment. The pressure could be adequately adjusted by constricting the descending aorta in the morphine group, but the heart would not tolerate complete adjustment to control levels in the animals receiving high halothane concentrations, the pressure being restored to only 44 mm Hg after 2.5% halothane.

CORONARY BLOOD FLOW. The myocardial flow in the halothane group decreased from 41 ml/100 gm myocardium/min to 31 ml following 2.5% halothane (Table; Fig 4). The baseline flow in the morphine group was 47 ml/100 gm myocardium/min, increasing to 59 ml after 3 mg/kg, 64 ml after 4 mg/kg, and 62 ml after 5 mg. These increases were significant when compared to the control value of the morphine group (paired t-test). The coronary flows following 3, 4, and 5 mg/kg of morphine were also significantly greater than flows after 1.0 and 1.5% halothane ($p < 0.05$).

Pressure adjustment did not significantly increase coronary flow in the halothane group; however, an increase in coronary flow was seen in the morphine group after 1, 2, and 3 mg/kg doses. The respective increases after pressure adjustment were from 46 ml/100 gm myocardium/min to 55, 49 ml to 59 ml, and 59 ml to 68 ml.

PERIPHERAL VASCULAR RESISTANCE. This was calculated using the formula:

$$\frac{\text{Mean arterial pressure} - \text{central venous pressure}}{\text{Cardiac output/kg}} = \frac{\text{mm Hg}}{\text{ml/min/kg}}$$

The baseline value in the halothane group was 91 mm Hg/ml/min/kg. A gradual decline occurred to 81 mm Hg/ml/min/kg after the 2.0% dose, and then there was a further drop to 62 at 2.5%. The control value in the morphine group was 67 mm Hg/ml/min/kg and gradually increased to 81 following 5 mg/kg of morphine except for one decreased value of 62 mm Hg/ml/min/kg, which occurred after the 2 mg dose.

CORONARY VASCULAR RESISTANCE. This was calculated using the formula:

$$\frac{\text{Mean aortic diastolic pressure} - \text{central venous pressure}}{\text{Coronary blood flow}} = \frac{\text{mm Hg}}{\text{ml/100 gm/min}}$$

The control resistance for the halothane group was 1.33 mm Hg/ml/100 gm/min. It increased to 1.37 after 0.5%, 1.48 after 1%, and then decreased to 1.2 after 1.5, 2.0, and 2.5% halothane. The morphine group control value was 0.85 mm Hg/ml/100 gm/min, which decreased to 0.6 following 1 mg of morphine and remained at that level for the rest of the experiment.

ARTERIAL pH, Po_2, Pco_2. The arterial pH in the halothane group varied from a control value of 7.35 to 7.54 after the 0.5% concentration. The morphine group pH was 7.39 initially and increased to 7.48 after the 3 mg/kg dose. The Po_2 ranged from 347 to 509 mm Hg in the halothane group and from 370 to 409 mm Hg in the morphine group. The Pco_2 varied from 18 to 26 mm Hg in the halothane group and from 21 to 26 mm Hg in the morphine group.

Comment

Halothane has been one of the most frequently used anesthetic agents and has been used extensively in anesthesia for heart operations. During the past several years, however, data have been obtained which demonstrate the deleterious effects of halothane on left ventricular contractility, cardiac output, and coronary flow. These effects are of obvious concern when dealing with patients having a diseased heart with already compromised myocardial function.

Vatner and Smith [9] have demonstrated a 68% reduction in myocardial contractility (dp/dt) with 2% halothane administration in animal experiments. This was accompanied by a decrease in arterial pressure and in coronary blood flow with 1 and 2% concentrations. They did not demonstrate a rise in late diastolic coronary resistance; however, Rusy and associates [5] found a 65% reduction in $\dot{Q}_{max}$ and a 29% decrease in the tension-time index following the administration of 1.5% halothane.

Weaver and co-workers [10] demonstrated a proportionate decrease in left ventricular contractility, myocardial work, regional blood flow, and coronary blood flow associated with halothane administration and related it to a reduction in myocardial oxygen consumption. The findings of Wolff and associates [11, 12] were similar, but they also implicated coronary vasoconstriction as a factor. Wyler [13] noted that peripheral vascular resistance does not change with halothane administration but that arterial blood pressure decreases and is related to diminishing cardiac output, cardiac work, and coronary flow.

Large clinical series using morphine as the major anesthetic agent for heart operations have been reported. Lowenstein and co-workers [3]

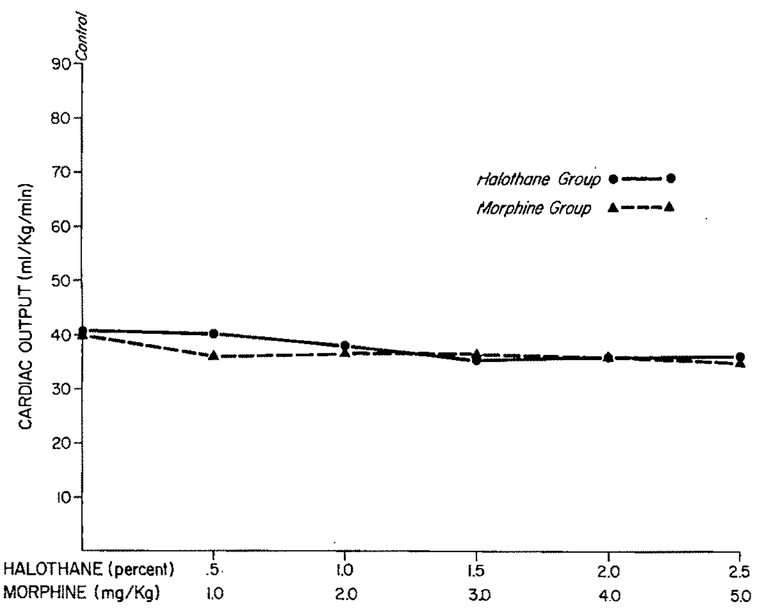

Fig 2. Cardiac output. The cardiac output was maintained essentially equal in both the halothane and the morphine group throughout the experiment.

found that morphine increases the cardiac and stroke indexes in patients who have depressed cardiac function preoperatively. Arens and colleagues [1] also noted the relative safety of morphine anesthesia in this group of patients. Vasko and associates [7] found that morphine increases ventricular contractile force, dp/dt, systolic ejection rate, and stroke power, but does so by stimulating sympathetic adrenal discharge. Henney and co-workers [2] demonstrated a transient decrease in peripheral vascular resistance following intravenous morphine administration and an increase in vascular space capacitance and venous pooling.

The effect of morphine on coronary blood flow is not well defined. Vatner and associates [8] found a decrease in coronary flow and coronary vasoconstriction following a 2 mg/kg dose of morphine in awake dogs. This was associated with a positive inotropic effect. The coronary vasoconstriction could be blocked by alpha-receptor blockade but not by beta blockade. Coronary vasoconstriction was not observed in previously anesthetized dogs or with administration of large doses of morphine (10 mg/kg). The coronary flow was measured by a Doppler ultrasonic flowmeter placed around the left circumflex coronary artery. However, Miller's group [4], using the radioactive microsphere technique, demonstrated significant increases in coronary blood flow following 2 mg/kg injections of morphine as well as a 166 to 176% increase in the fraction of cardiac output going to the coronary circulation. The microspheres were 50μ in size and were injected into the left ventricle.

Because of the depressant effects of halothane on the myocardium and the indirect stimulating effect of morphine on cardiac output, it was elected to control cardiac output by bypassing the right ventricle at a constant rate, thus decreasing the variability of left ventricular work and its effects on coronary flow. Equalization of mean blood pressure was also attempted in order to eliminate this variable. Coronary blood flow was found to be significantly increased from control values following 3, 4, and 5 mg/kg doses of morphine without pressure adjustment. This was accompanied by a decrease in coronary vascular resistance. This study, therefore, supports the findings of Miller and associates [4], who also noted increased coronary flow during morphine anesthesia. Their study was performed with rather large microspheres, however, and the microspheres were injected into the left ventricle, which can cause streaming and could perhaps lead to artificially high values.

The findings of Vatner and colleagues [8], who noted increased coronary vascular resis-

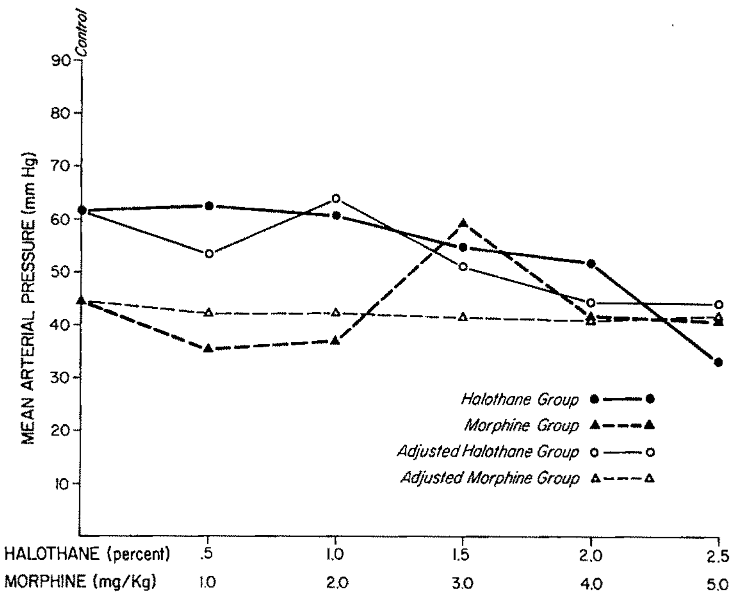

Fig 3. Mean arterial pressure. The pressure in the halothane group was slightly higher than that of the morphine group at most determinations.

tance with morphine, were not substantiated by our study. However, anesthesia in the animals in the present experiment was initially induced with sodium thiopental, and Vatner's preanesthetized group did not demonstrate increased coronary resistance. Their flow data were obtained from the left circumflex coronary artery only and by Doppler ultrasound, whereas the coronary flow in this study was the total coronary sinus output measured by a right ventricular sump. Adjustment of the aortic root pressure toward control values only moderately increased coronary flow in the morphine group and was not a major factor.

The coronary flow in the halothane group did not decrease as much as other studies have indicated. This is probably due to the maintenance of a constant cardiac output in our study, supporting the concept that much of the decrease in coronary flow seen with halothane is secondary to decreased cardiac output and cardiac work. Coronary vascular resistance increased only slightly in the halothane group.

Although the right heart bypass model allows control of cardiac output, it does create some problems. The rate of pump flow was determined by the initial flow of blood from the dog to the pump. Following a period of stabilization this flow was maintained for the duration of the experiment. The cardiac outputs thus arrived at were somewhat low, but not so much as to create acidosis. In spite of the disadvantage of the lower cardiac output, this technique did serve to maintain a very consistent cardiac output in each animal. Although all animals had hemodilution, the decrease in vicosity was not so large as to prevent a progressive increase in peripheral vascular resistance in the morphine group.

The mean arterial pressure during the pretreatment period in the morphine group was substantially lower than that of the halothane group (45 versus 62 mm Hg), and both were below normal. The reason for the difference in pressure is not known. However, cardiac output and coronary flow in the two groups were quite similar. In spite of the lower arterial pressure in the morphine group, the coronary flow was significantly higher than in the halothane group at several of the dose levels. The effects of morphine on venous pressure could not be examined in this model because of the use of gravity venous drainage into the pump system, which resulted in venous pressures of zero.

Coronary flow is normally quite responsive to left ventricular work, but in this experimental model cardiac work remained constant except during the 3 mg/kg morphine dose, when the mean pressure increased secondary to an increase in peripheral vascular resistance. The in-

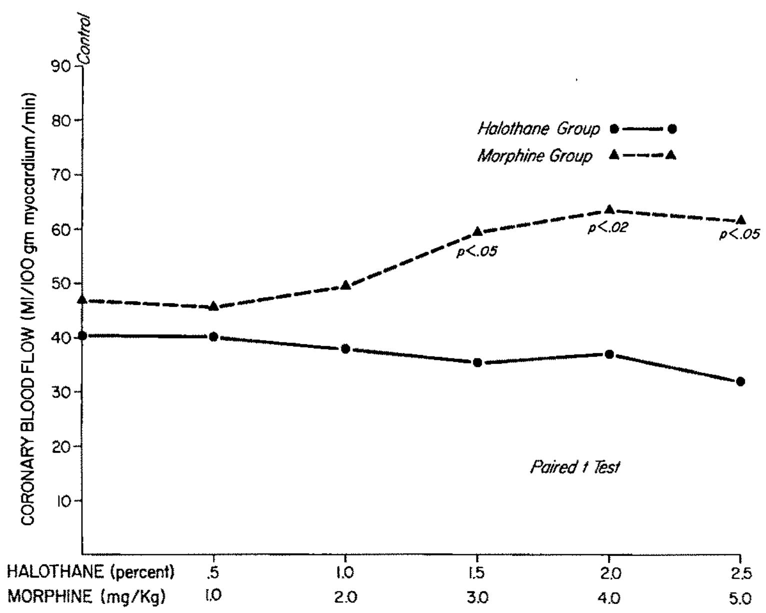

Fig 4. Coronary blood flow. Significant increases in coronary flow occurred in the morphine group after 3, 4, and 5 mg/kg doses when compared to the morphine control value (paired t-test). In contrast, flow in the halothane group decreased slightly with increasing concentrations of the anesthetic.

Coronary Flow before and after Pressure Adjustment at Varying Concentrations of Halothane or Morphine Anesthesia

Anesthesia & Dosage	Coronary Flow[a]	Coronary Flow[a] with Pressure Adjustment
Halothane (%)		
Control	41	. . .
0.5	40	30
1.0	38	41
1.5	35	35
2.0	37	39
2.5	31	40
Morphine (mg/kg)		
Control	47	. . .
1	46	55
2	49	59[b]
3	59[c]	68[d]
4	64[d]	62[c]
5	62[c]	68[d]

[a] ml/100 gm myocardium/min.

[b] $p < 0.005$ (paired t-test).

[c] $p < 0.05$ (paired t-test).

[d] $p < 0.02$ (paired t-test).

crease in coronary flow in the morphine group did not therefore appear to be related to left ventricular work. In both groups the heart rate decreased moderately, thus increasing the diastolic time during which most coronary flow occurs. This could account for some of the increased coronary flow in the morphine group, but it did not increase the flow in the halothane group.

Morphine administration therefore increases coronary blood flow when the cardiac output is maintained at a constant level, whereas little change occurs in coronary flow following halothane administration until high doses are reached. Further studies are planned to clarify the hemodynamic effects of morphine on coronary flow without the use of right heart bypass and controlled cardiac output. These will include measurement of myocardial oxygen consumption, regional myocardial blood flow, cardiac output, and left ventricular contractility. The enhancement of coronary flow by morphine as demonstrated in this study should give more support to its use as an anesthetic agent in patients with heart disease.

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Resuscitation of the Moribund Patient Using Portable Cardiopulmonary Bypass

Kenneth L. Mattox, M.D., and Arthur C. Beall, Jr., M.D.

ABSTRACT **The advancements in extracorporeal cardiopulmonary support through oxygenation and pumping units have permitted the explosive development of heart surgery. A battery-powered portable cardiopulmonary bypass machine has been used in 39 patients whose condition precluded transport to the operating room. Nineteen patients with massive pulmonary emboli, 10 with extensive cardiopulmonary trauma, 2 who had sustained massive drug overdose, and 2 with cardiogenic shock from acute myocardial infarction were successfully placed on cardiopulmonary bypass at the bedside within 15 minutes of cardiac arrest using femoral artery and femoral vein cannulation. Six patients who had cardiac arrest and suspected massive pulmonary emboli were found to have no mechanical cause for their arrest.**

Thirteen of the patients with massive pulmonary emboli were saved. Eight of the 10 patients who required portable cardiopulmonary bypass for massive traumatic thoracic injuries had control of hemorrhage and repair, allowing bypass to be discontinued. Two of these 8 patients had sustained transection of the proximal left anterior descending coronary artery. Sixteen patients survived for more than 30 days, and there are 15 long-term survivors.

Although LeGallois [11] in 1813 proposed the concept of artificial cardiopulmonary support through oxygenation of the blood, actual implementation of this technique awaited the discovery of heparin by Howell and Holt [10] in 1918. Gibbon never had the opportunity to treat a moribund patient with pulmonary emboli, but it was such a patient that prompted him to begin developmental work in 1932 which resulted in the first successful clinical intracardiac operation using cardiopulmonary bypass in 1953 [9]. Between 1950 and 1975, multiple engineering and technical advances were made in both cardiopulmonary bypass equipment and operative techniques requiring these modalities. The modern heart-lung machine with its DeBakey roller pump and its oxygenators of bubble, disc, or membrane configuration allows the cardiothoracic surgeon a wide range of operations that were previously impossible. With the development of a portable pump oxygenator, the concept of artificial cardiorespiratory support has been extended to disease entities which require initiation of cardiopulmonary bypass prior to transport to the operating room [1].

Methods

During the early 1960s a compact, portable, battery-operated roller pump was developed at the Cora and Webb Mading Department of Surgery, Baylor College of Medicine [4]. This early unit was employed until 1969, when a Travenol* portable cardiopulmonary bypass unit was adopted. The use of this portable cardiopulmonary support unit is considered in moribund patients who do not respond to the usual resuscitative measures.

The portable cardiopulmonary unit is moved to the bedside during resuscitation and evaluation. This battery-operated, portable pump oxygenator uses a disposable 6-liter plastic oxygenator bag and is always assembled but not primed. A special sterile instrument pack containing the following items is kept with the unit.

Surgical knives with blades (3)
Scissors—including Pott's vascular (3)
Self-retaining retractors (Gilpe) (3)
Peripheral vascular clamps (6)
Vascular forceps (3)
Umbilical tape

From the Cora and Webb Mading Department of Surgery, Baylor College of Medicine, and the Ben Taub General Hospital, Houston, TX.

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Address reprint requests to Dr. Mattox, 1502 Taub Loop, Houston, TX 77030.

*Travenol Laboratories, Inc., Morton Grove, IL.

Assorted sutures
Assorted hemostats
Femoral artery perfusion cannulas
Assorted small retractors
Towel clips
Pump clamps (2)

Extra potentially needed equipment is kept on a cart accompanying the pumping unit:

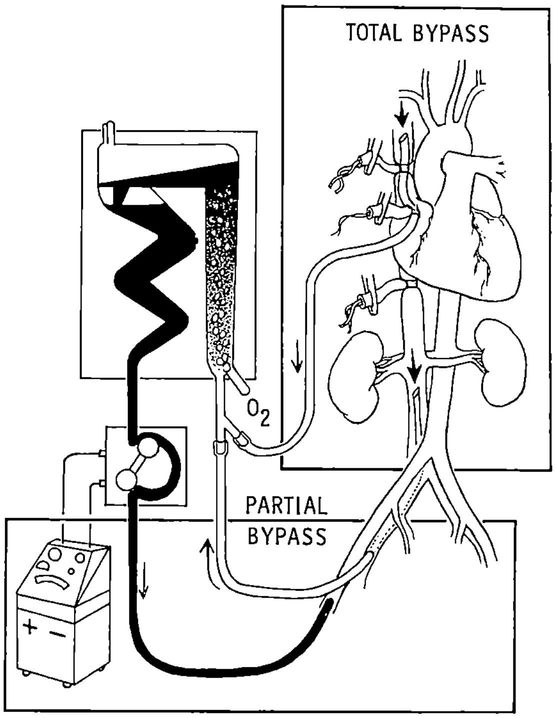
Extra oxygen bottle
Six 1,000 ml bags of 5% dextrose in water
Extra pump clamps
Heparin
Sterile cannulas, arterial and venous
Local anesthesia
Prep kit and razors
Soap and antiseptic solution
Sterile drapes
Sterile gloves
Electric extension cord
Asepto syringes
Foley catheter
Intravenous tubing and needles
Selected drugs
Laboratory tubes

Routine cardiopulmonary resuscitation is continued during cannulation. In a hypotensive patient with suspected massive pulmonary embolus, cardiopulmonary bypass occasionally may be instituted prior to angiography for support during transportation and radiographic evaluation.

Senior surgery residents on duty in the hospital 24 hours a day are skilled in performing femoral artery and femoral vein cannulation and in priming the bubble oxygenator. Total-body heparinization (3 mg per kilogram of body weight) is used unless the patient's weight is not known, in which case 20,000 units of beef lung heparin is administered. An additional 2,000 units of heparin is placed in the oxygenator bag after it has been primed with 1,500 ml of 5% dextrose in water [6]. Should clot be encountered in the femoral vein of the patient with a pulmonary embolus, the femoral artery is cannulated first and then the cannula is used to displace the clot from the femoral vein up the inferior vena cava into the lungs. This procedure compounds an already existing pulmonary embolus, but it allows for institution of mechanical cardiopulmonary support. Flow rates averaging 3,700 ml per minute are achieved, with return equaling that which is received. Blood or additional prime is added to the pump as needed. Positive pulmonary ventilation is continued to prevent overdistention of the lungs. An in-line heat exchanger is routinely used.

Sterility is maintained while a transfer board fitting the pump frame is positioned below the patient. Although the pump oxygenator has a self-contained battery mode, it is connected to a regular 110-volt line in the radiology department, in the operating room, or during cardiac catheterization. Following open thoracotomy, the circuit is converted to total cardiopulmonary bypass using the Y-connector and cannula passed through the right atrial appendage into the superior vena cava (Figure). Umbilical tapes are passed around the superior and inferior venae cavae using catheter tourniquets or caval clamps. Inflow occlusion is achieved, allowing for all venous return to drain into the pump oxygenator. Appropriate operative procedures

Femoral vein–femoral artery partial bypass with conversion to total bypass.



such as pulmonary embolectomy, coronary artery bypass, and repair of injuries to the pulmonary artery, pulmonary vein, ascending aorta, and the heart itself may be performed. Liberal use of albumin, Lasix, and positive end-expiratory pressure, even during total cardiopulmonary bypass, aids in the prevention of alveolar flooding and the subsequent production of postperfusion respiratory insufficiency. Following appropriate operative procedures, cardiopulmonary bypass is discontinued and heparin is neutralized with protamine sulfate given in a dosage of 4.5 ml per kilogram of body weight or in a ratio of 1.5 mg per 100 units of heparin if the patient's body weight is not known. A rapid test to assess heparin neutralization and one which is available in the operating suite is the activated clotting time [13]. Arteriorrhaphy, venorrhaphy, ligation of the vena cava, or other appropriate procedures are performed as indicated.

Clinical Material

During the past 7 years, portable cardiopulmonary bypass was instituted in 39 moribund patients at the Ben Taub General Hospital. Among these 39 patients, 19 had massive pulmonary embolus, 6 had gunshot wounds to the chest, 3 had stab wounds to the chest, 2 had massive drug overdose, 2 were in cardiogenic shock secondary to myocardial infarction (which occurred during cardiac catheterization), 1 was a victim of massive blunt trauma, and in 6 patients no mechanical or chemical etiology for their arrest was found (Table 1). For 3 other patients with massive hemoptysis the portable pump was available on standby concomitant with control of their airway.

Portable cardiopulmonary bypass was instituted at the patient's bedside on the hospital ward in 21 cases, the emergency center in 11 cases, the operative suite on 5 occasions, and in the cardiac catheterization laboratory on 2 occasions. The portable unit was employed in the 5 bypass procedures instituted in the operating suite because of the urgency of the situation, the availability of the portable pump and its ease of operation, as well as because of the remote necessity of having to transfer the patient for radiological evaluation. In all but 2 cases, cardiopulmonary bypass was instituted prior to arrival of the extracorporeal perfusion technician.

Among the 10 patients with massive thoracic trauma, 2 had extensive tracheobronchial injury, 2 had extensive injury to the pulmonary veins or arteries, and 5 had cardiac injuries; none of these patients could be resuscitated by routine measures. Among the 19 patients with massive pulmonary embolus were 8 patients with gynecological entities for which operative procedures had been performed. Two other patients came to the emergency center with a history of having been on birth control pills and sustained a cardiac arrest during their early

Table 1. Results among 39 Moribund Patients Resuscitated with Portable Cardiopulmonary Bypass

	Died in OR		Died in ICU			
Diagnosis	On Pump	Off Pump	<30 Days	>30 Days	Went Home	Total
Massive pulmonary embolus	1	2	3	0	13	19
Trauma	2	2	4	1	1	10
Drug overdose	2	0	0	0	0	2
Myocardial infarction	2	0	0	0	0	2
Cardiac arrest (no mechanical or chemical diagnosis)	0	3	2	0	1	6
Total	7	7	9	1	15	39

OR = operating room; ICU = intensive care unit.

evaluation; 4 patients had recently undergone cholecystectomy; 2 patients had recent multiple trauma; 2 patients had orthopedic problems, and 1 patient was under evaluation for abdominal pain. Both patients with cardiogenic shock had left main coronary artery lesions and were undergoing heart catheterization when cardiac arrest ensued, and routine resuscitation did not lead to return of cardiac activity. One of the patients with massive drug overdose had taken 50 propranolol tablets (500 mg), and the other had asystole following illicit intravenous injection of multiple unknown drugs. This second patient was fully awake upon arrival at the emergency center, although cardiac output was being maintained by external cardiac massage by emergency medical technicians.

Six patients were thought to have pulmonary emboli and, being in a moribund condition and not responding to routine resuscitation, were placed on portable cardiopulmonary bypass. During evaluation in the cardiac catheterization laboratory no demonstrable disorder—be it pulmonary emboli or stenotic lesions of the coronary arteries—was found on special roentgenograms. These patients ranged in age from 18 to 65 years. Following a period of 3 to 6 hours cardiopulmonary bypass was discontinued.

Results

Among 39 moribund patients undergoing portable cardiopulmonary bypass for essentially fatal diagnoses or conditions, 15 are long-term survivors and are alive and well up to 9 years later (see Table 1). One additional patient died more than 30 days postoperatively of hypoxic brain symptoms secondary to prolonged shock and hypoxia prior to the time of his arrival at the emergency center. He had a concomitant injury to his heart and left anterior descending coronary artery. Twenty-six patients had successful control of their injuries and cardiac output satisfactory enough to allow for discontinuance of cardiopulmonary bypass. Four of this group, 2 with massive pulmonary emboli and 2 with traumatic injuries, died in the operating room as a result of complicating illnesses or coagulopathies. Seven patients died in the operating suite while still on cardiopulmonary bypass. The use of portable cardiopulmonary bypass equipment was most successful in the patients with massive pulmonary emboli (see Table 1), and this has been previously reviewed [3]. Both patients with massive drug overdose failed to respond to cardiotonic drugs or cardiac pacing and died.

Among the 6 patients in whom no etiology for their arrest was found, 3 died of low cardiac output immediately upon discontinuance of pump support. One patient died 21 days after cardiorespiratory support of a second catastrophic event. Postmortem examination failed to reveal the etiology of her cardiorespiratory failure. One patient died 4 days following discontinuance of cardiorespiratory support, never having regained consciousness or recovered from a low cardiac output state. The sixth in this group of patients in whom a mechanical diagnosis was not made is still surviving and doing well.

Twelve patients with major complications later died. The complications after bypass among the 26 patients in whom cardiopulmonary support was discontinued have some direct correlation with the use of the pump (Table 2). This fact should not, however, discourage an aggressive approach to resuscitation, for without extracorporeal cardiorespiratory support none of the patients in this series would have been salvaged. The intraoperative appearance of copious fluid in the endotracheal tube and the presence of postoperative respiratory insufficiency has prompted early use of positive end-expiratory pressure, diuretics, and albumin.

Table 2. Complications among 26 Patients in Whom Cardiopulmonary Bypass Was Discontinued

Complication	No. of Patients
Respiratory insufficiency	12
Pulmonary edema	7
Low cardiac output	3
Depressed CNS activity	2
Coagulopathy	2
Recurrent pulmonary embolus (IVC not ligated)	1
Anastomotic aneurysm—saphenous bypass graft	1

CNS = central nervous system; IVC = inferior vena cava.

Case Histories

The approach to resuscitative cardiopulmonary bypass is demonstrated by the case histories of 3 individuals. The first, a 22-year-old Latin American man, sustained a stab wound to the left chest and was initially admitted to an outlying hospital in a hypotensive state. He was promptly transferred to the Ben Taub General Hospital, where he arrived approximately 40 minutes after his injury with asystole but with intact cerebral function. Resuscitative thoracotomy, relief of cardiac tamponade, and internal cardiac massage were performed, and the patient became awake and combative, requiring morphine anesthesia and succinylcholine. Following control of hemorrhage with appropriately placed sutures, the right ventricle was noted to contract; however, the left ventricle was dark and noncontractile, and an injury to the proximal left anterior descending coronary artery was noted. With internal cardiac massage continuing, portable cardiopulmonary bypass was instituted in the shock room and the patient underwent emergency saphenous vein bypass grafting from the ascending aorta to the left anterior descending coronary artery with ligation of the lacerated ends of the coronary artery. Following release of the aortic clamp approximately three hours after the injury, the left ventricle began to contract vigorously. The patient had a moderately complicated postoperative course which included respiratory insufficiency, upper gastrointestinal bleeding, and an anastomotic aneurysm at the distal suture line of the saphenous vein graft that required reoperation for repair.

The second case is that of a 35-year-old white woman who underwent hysterectomy and was preparing to go home on the sixth postoperative day when she suddenly collapsed at her bedside. An initial blood pressure of 40 mm Hg systolic could not be improved with the administration of vasopressors and oxygen supplementation through an endotracheal tube. The arterial Po_2 was measured at 35 mm Hg, and an electrocardiogram revealed marked right axis deviation. As the Thoracic Surgery Service was being called, the patient sustained cardiac arrest and could not be defibrillated. External cardiac massage was continued as femoral artery and vein cannulation was performed. Within 15 minutes the patient was on portable cardiopulmonary bypass with a flow rate of 3,200 ml per minute, and arterial Po_2 on the pump was 320 mm Hg. She was transferred to the angiographic facility adjacent to the operating room, where a massive pulmonary embolus was documented. Pulmonary embolectomy was accomplished with removal of clots from the right, left, and main pulmonary arteries through embolectomy techniques previously described [1]. Following closure of the arteriotomy, the heart resumed a normal sinus rhythm with a normal right heart pressure. Cardiopulmonary bypass was discontinued, the inferior vena cava and left ovarian veins were ligated, and she was discharged from the hospital on the seventh day following her cardiac arrest.

The third case history is that of an 18-year-old Latin American woman who had had a laparotomy for a ruptured uterus occurring during active labor 2 days previously. She was transferred to the Ben Taub General Hospital with virtually no blood pressure and an elevated central venous pressure; 5 minutes after arrival she sustained a cardiac arrest. Routine resuscitative measures were unsuccessful, and she was placed on portable cardiopulmonary support. A pulmonary angiogram revealed no pulmonary emboli to be present. She was transferred to the operating room where, by using appropriate cardiotonic drugs and judiciously returning the pump fluid to the patient, she was taken off cardiopulmonary bypass while maintaining a normal sinus rhythm and a good cardiac output. She had no respiratory insufficiency after bypass and returned to a normal life. The etiology of her arrest was thought to be a combination of electrolyte imbalance, sepsis, hypovolemia, oversedation, and hypoxia.

Comment

Early cardiac surgeons were desirous of providing cardiorespiratory support for the patient in a moribund condition from acquired disease. It was not until 1961 that the first successful pulmonary embolectomy in a moribund patient with a massive pulmonary embolus was managed under cardiopulmonary bypass [5]. The development of a disposable bubble oxygenator, nonblood primes, and battery-operated roller pumps has made resuscitative cardiopulmonary bypass available and more applicable in emergency situations. Emergency portable cardiopulmonary bypass has only recently been applied to the victims of massive trauma or of accidental hypothermia [7, 8, 12]. It is, however, a rare patient with massive cardiothoracic trauma, massive pulmonary embolism, acute myocardial infarction, or cardiac depression from a variety of miscellaneous conditions (sepsis, massive drug overdose, complicated electrolyte imbalance) in whom cardiorespiratory support with extracorporeal devices is the only means of salvage [2, 14].

Use of portable cardiopulmonary bypass requires specific precautions, including an in-line heat exchanger with a rewarming unit, careful anticoagulation of the patient and the pump prime, availability of an additional small portable oxygen cylinder, proper battery maintenance, and special instrument packs. With a rehearsed plan of action and previously assigned tasks to members of the team, the aggressive approach of resuscitative cardiopulmonary bypass produces satisfactory results.

A patient's diagnosis may be straightforward, as it was in the first case history, and transportation from the emergency center directly to the operating room is possible. However, in patients in whom the diagnosis is not apparent, pulmonary or coronary angiography or both is essential. Should there be no documented reversible intrathoracic disorder, such as coronary artery occlusion, massive pulmonary embolus, acute aortic valve insufficiency, acute ventricular septal defect, left atrial myxoma, or similar condition, unnecessary thoracotomy may be prevented, as was shown in the third case history. Although the situation is complicated by ethical and medicolegal considerations, the surgeon must have a plan of action for those patients in whom there is no demonstrable reversible surgical cause for cardiorespiratory collapse. In a few patients, cardiorespiratory support with a portable pump may allow for reversal of certain medical conditions such as sepsis, electrolyte imbalance, and cardiac depression secondary to drugs. Patients with cardiac depression secondary to drug overdose might profit from the inclusion of a renal dialysis unit in the extracorporeal cardiopulmonary bypass circuit.

Resuscitation involves applying the techniques and equipment available to the treating physician. Many community hospitals and most general hospitals now possess cardiopulmonary bypass equipment. Such equipment can now be fitted with a portable battery pack delivering adequate power for transportation from one hospital location to another. The limits of the art of resuscitation may be extended by the application of portable extracorporeal cardiorespiratory support to the moribund patient.

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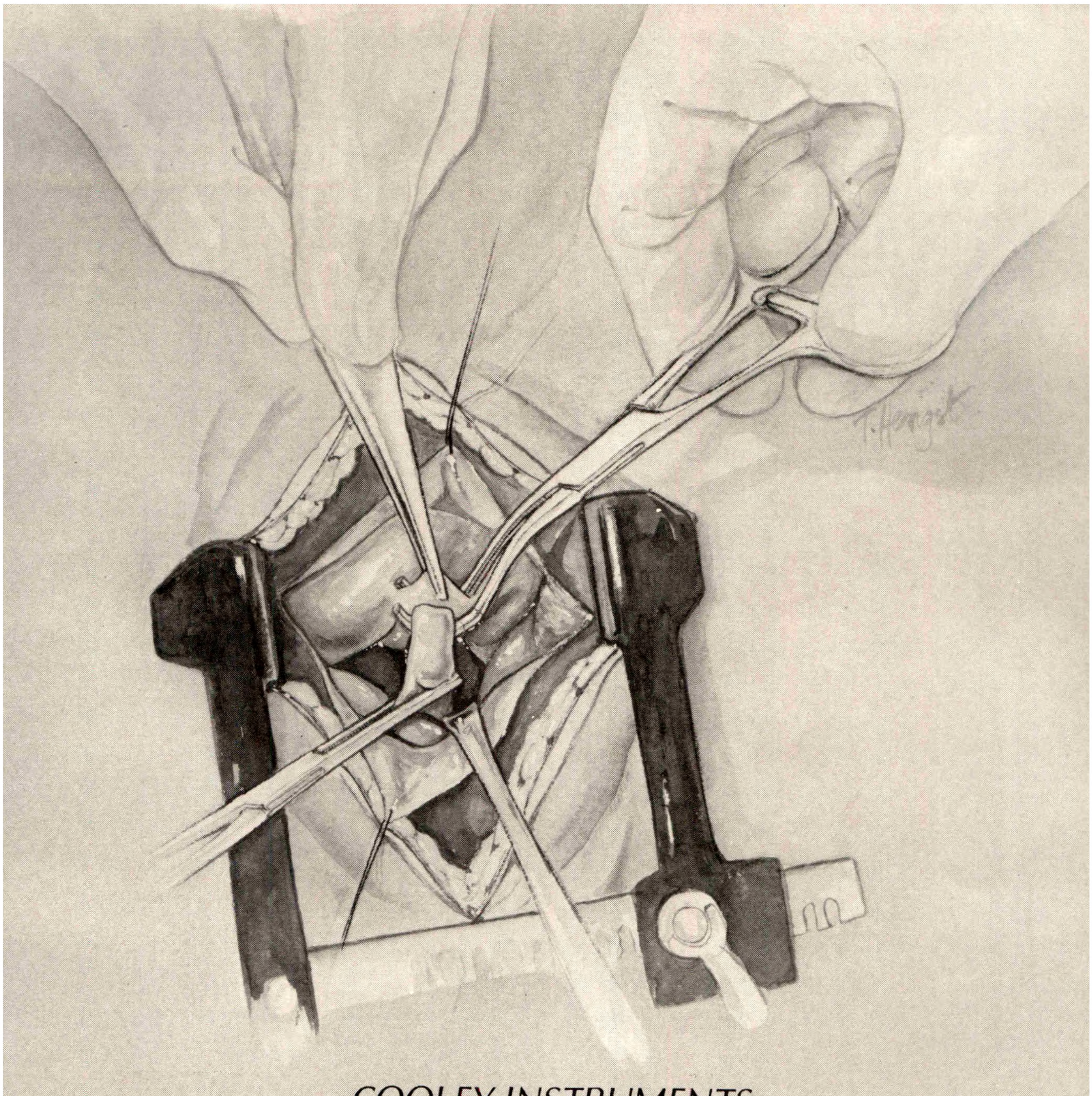

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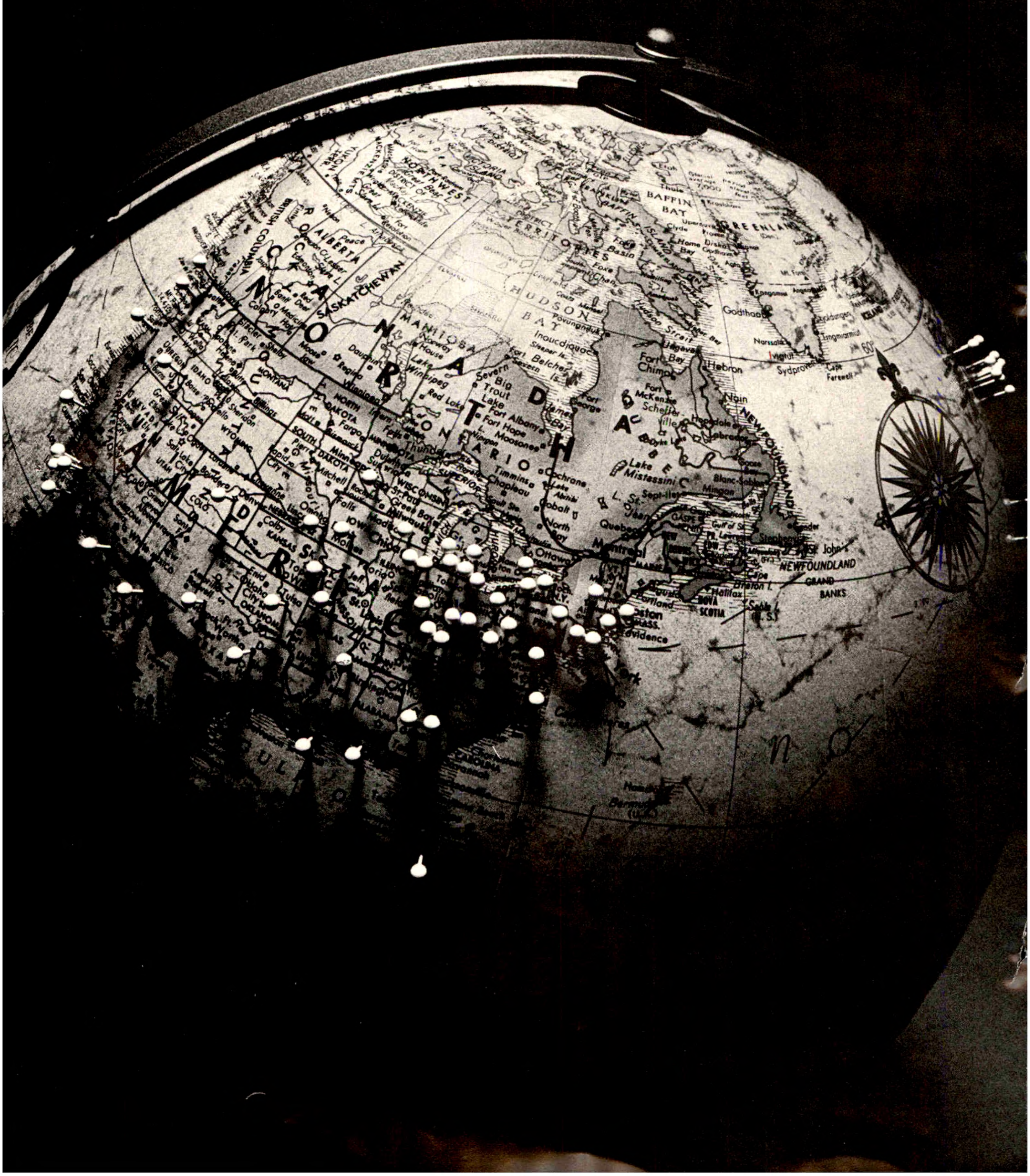

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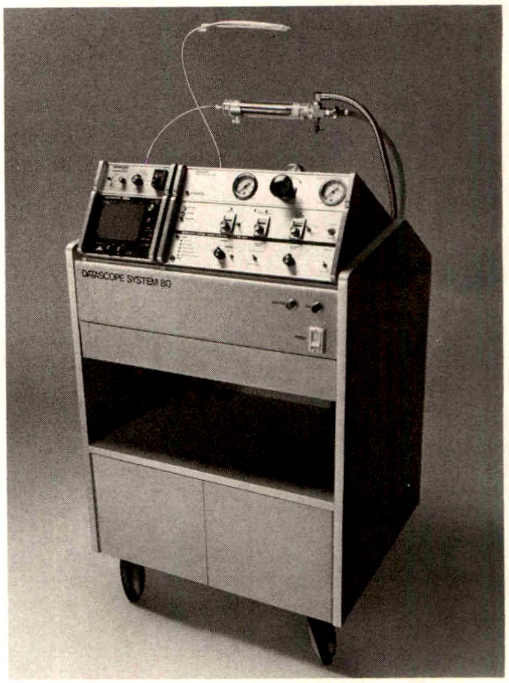

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*U.S. Patent #3692018

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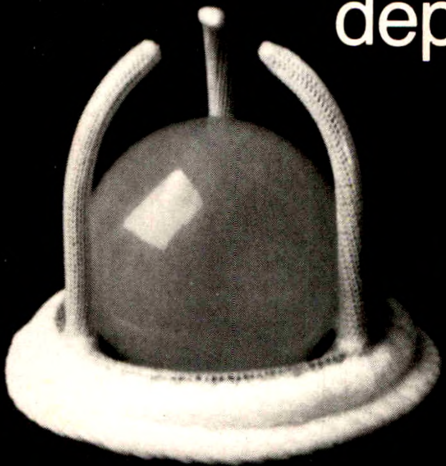

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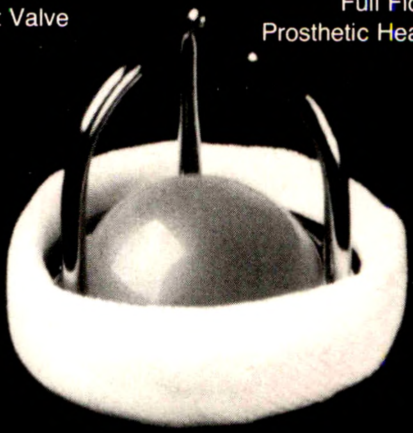

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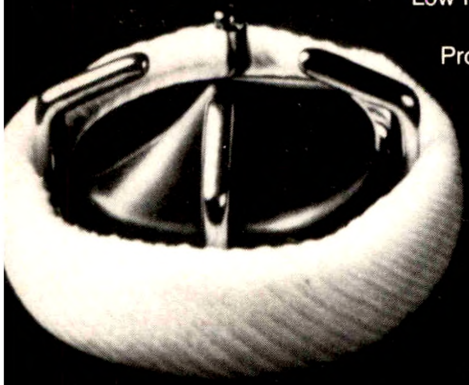

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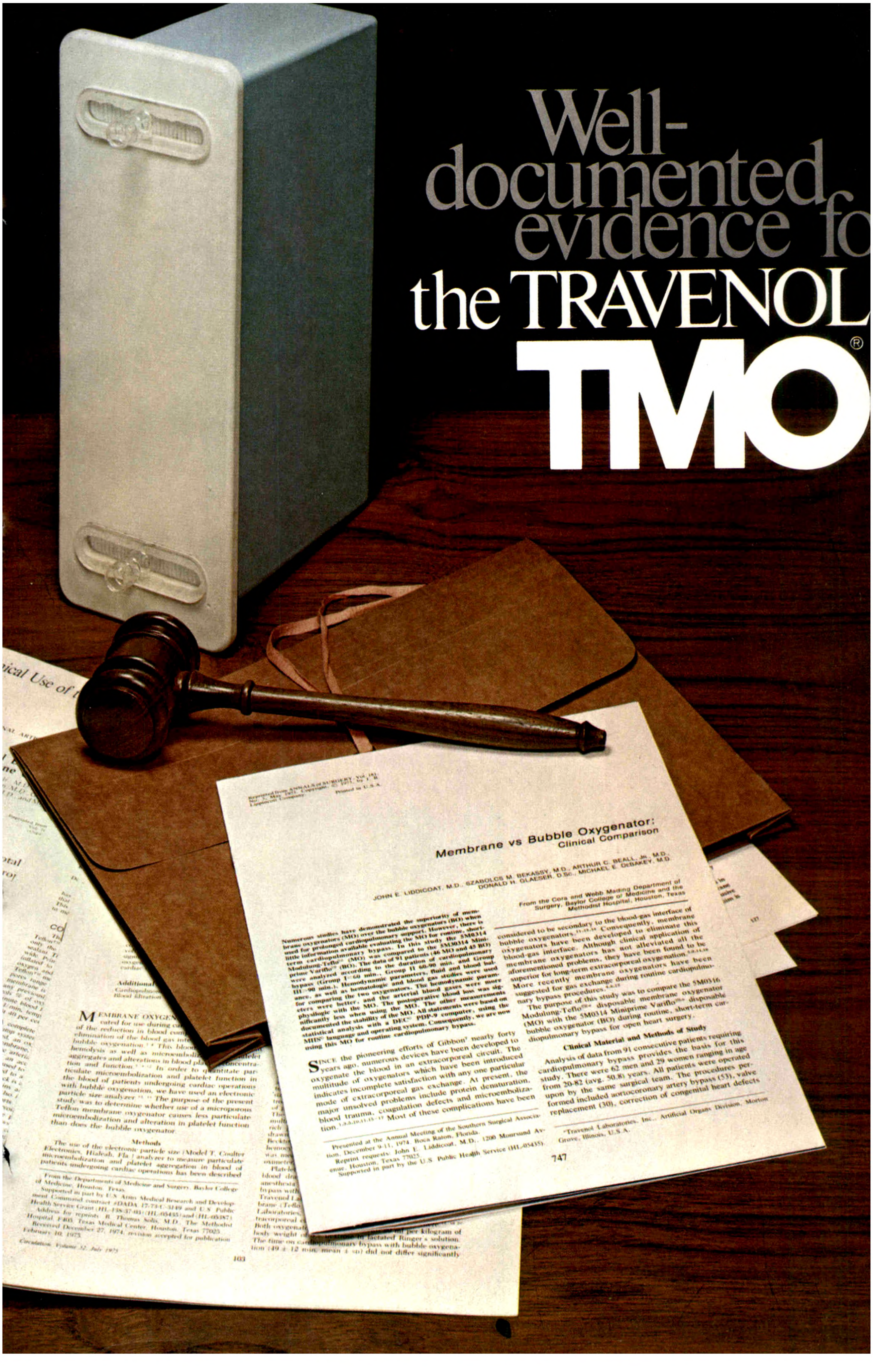
Well-documented evidence fo
the TRAVENOL
TMO®
Membrane vs Bubble Oxygenator:
Clinical Comparison
JOHN E. LIDDICOAT, M.D., SZABOLCS M. BEKASSY, M.D., ARTHUR C. BEALL, JR., M.D., DONALD H. GLAESER, D.Sc., MICHAEL E. DEBAKEY, M.D.
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Methods
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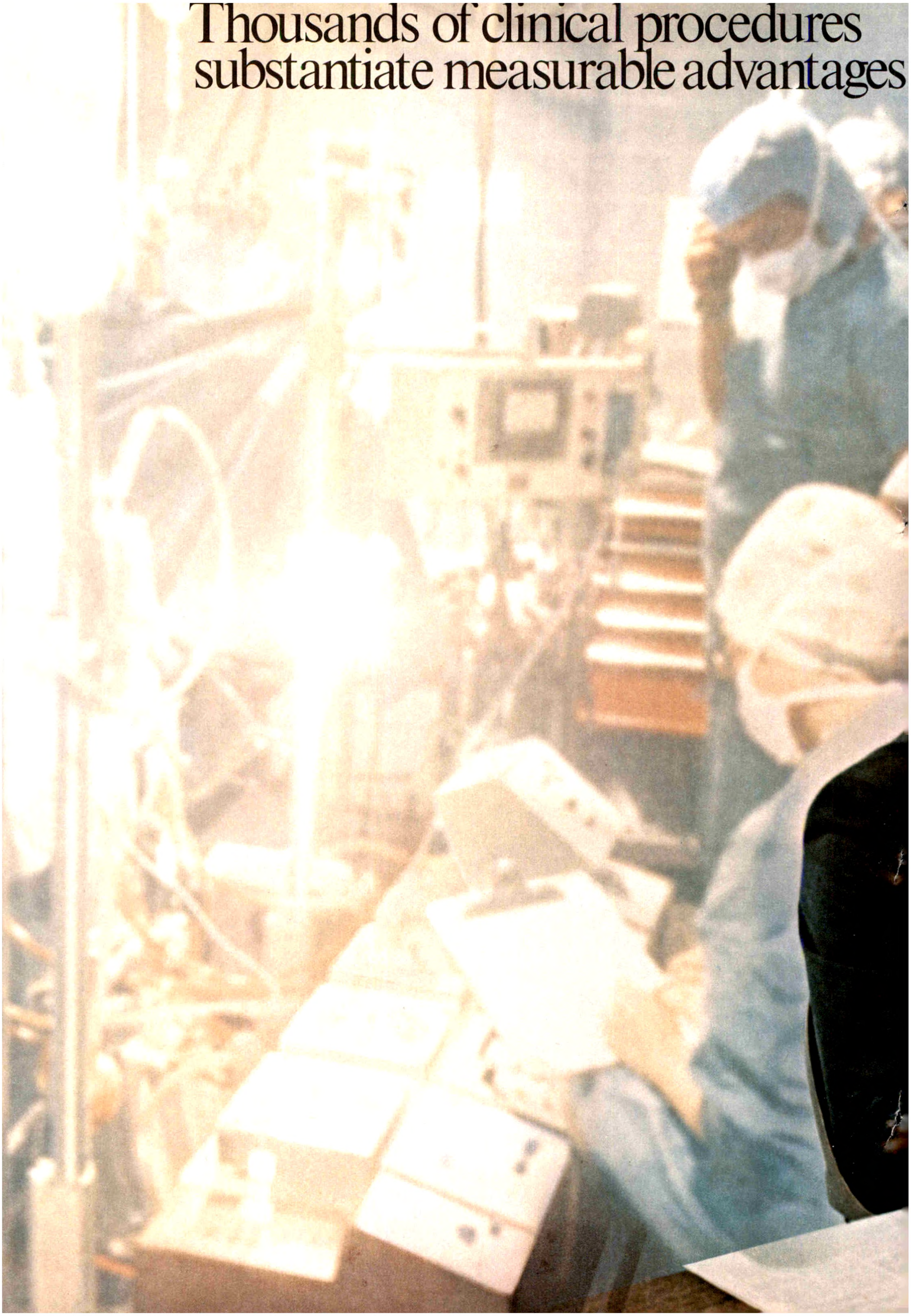

for the Travenol TMO® Membrane Oxygenator

Since the introduction of the Travenol TMO Membrane Oxygenator, surgeons have devoted significant effort to clinical evaluations of this gas exchange device used during cardiopulmonary bypass. Independent teams led by Berry and DeBakey reported that the TMO oxygenator produced less trauma to the blood than bubble oxygenators.[1,2] Solis credited it with better maintenance of platelet function.[3] According to the experience of Heimbecker et al, the unit contributed to lower levels of plasma hemoglobin during bypass and higher platelet survival rates. He also reported reductions in postoperative bleeding (chest drainage) and the need for banked blood.[4] Of major significance is the evidence submitted by Liddicoat et al verifying that the TMO oxygenator provided superior performance during cardiopulmonary bypass when compared to bubble oxygenators.[5]

The Travenol TMO Membrane Oxygenator provides these advantages at costs comparable to bubble oxygenators. In addition, gas transfer across the membrane eliminates oxygenator-created microbubbles. This method of gas exchange within the TMO Membrane Oxygenator more closely resembles that of the normal human lung and will permit independent control of oxygen and carbon dioxide transfer. The oxygenator is designed to operate at blood flow rates up to 6 liters per minute and, under standard test conditions, will transfer 300 ml of oxygen per minute.

Copies of the previously mentioned papers and those others listed pertaining to the TMO Membrane Oxygenator are available upon request from your Travenol Cardiopulmonary Systems Specialist.

The Travenol TMO Membrane Oxygenator is the unit formerly referred to as the Travenol MODULUNG-TEFLO Membrane Oxygenator.

References
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Additional references on page 4.

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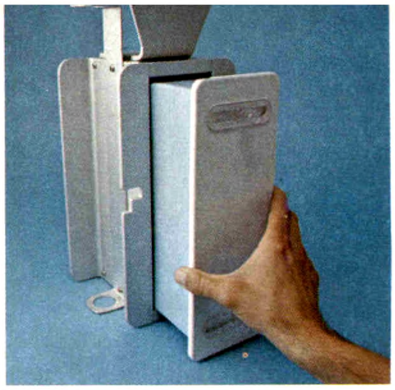
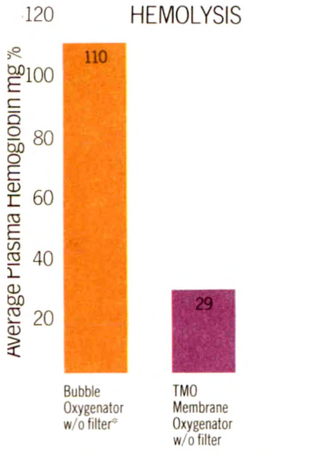


the Travenol TMO® Membrane Oxygenator... performance you can count on



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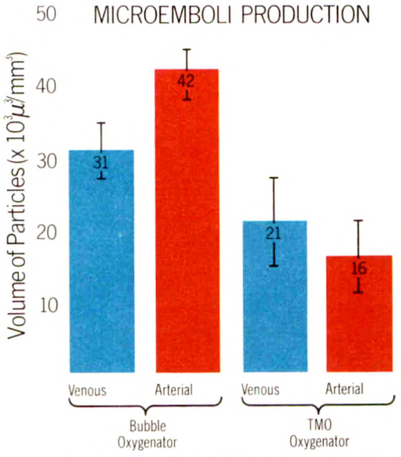
No. of cases—TMO Oxygenator 65
Bubble Oxygenator 70

*Bubble oxygenator w/filter—peak hemolysis 200 mg %



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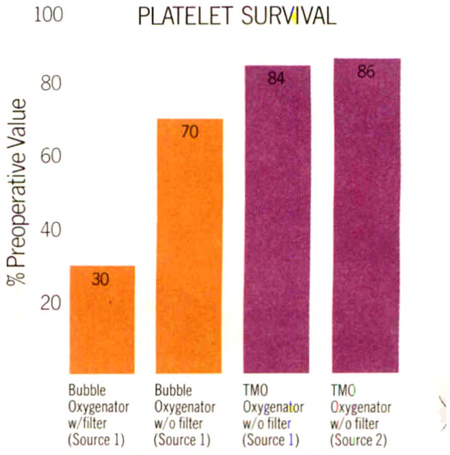

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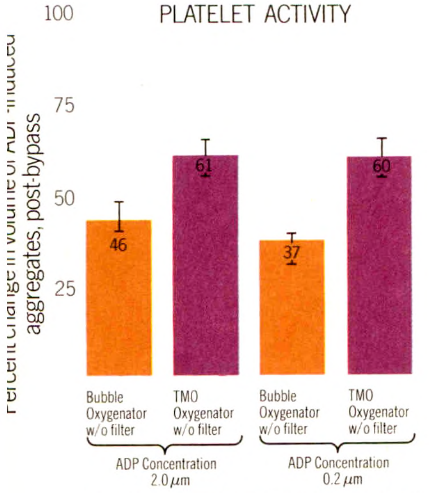

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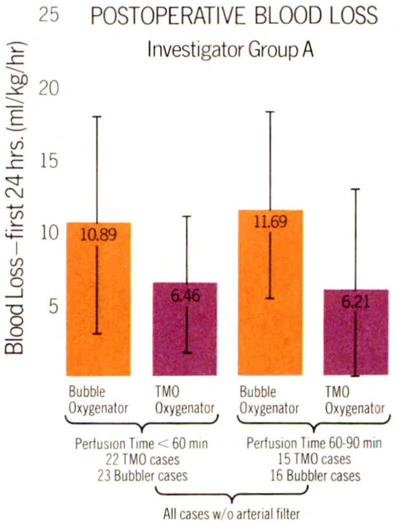

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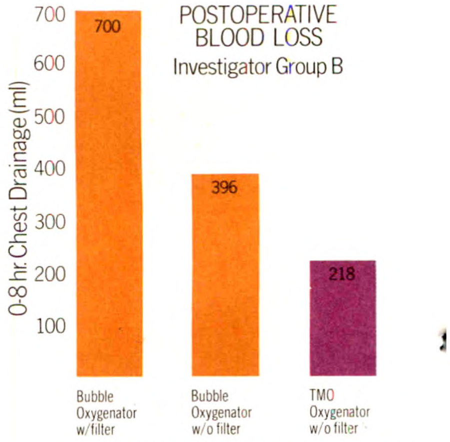

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INDICATIONS

The Travenol TMO Membrane Oxygenator is indicated for the oxygenation of blood and the removal of carbon dioxide from it in an extracorporeal circuit during total cardiopulmonary bypass at flow rates up to 6 liters/minute at altitudes not in excess of 2400 feet (730 meters).

CONTRAINDICATIONS

Selection of patients as candidates for oxygenation is totally a medical responsibility and the outcome is dependent on many variables, including patient pathology and surgical and perfusion procedures.

WARNINGS

Evaluation of this oxygenator at elevated altitudes has shown inadequate outlet partial pressure for total bypass (apparently because of lower O_2 partial pressure differences across the membrane). Until appropriate modifications are made, use of this device at altitudes above 2400 feet (730 meters) is not recommended.

In patients who are actively bleeding, medical judgment must be exercised in the use of the device. Benefits of oxygenation must be weighed against risks of total body heparinization. Oxygen requirements and transfer rates are influenced by many variables during perfusion.

Use of blood suction devices must be limited where possible.

PRECAUTIONS

Adequate heparinization is essential. If the oxygenator is used in hyperbaric environments, both sides of the oxygenator must be referenced to the same pressure. The gas outlet port should remain open and free of any obstructions.

Before using, refer to complete directions accompanying the product.

Additional references (continued from previous page)

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Travenol Laboratories, Inc. 10/76

The Surgical Treatment of Wolff-Parkinson-White Syndrome: Evolution of Improved Methods for Identification and Interruption of the Kent Bundle

Will C. Sealy, M.D., John J. Gallagher, M.D., and Andrew G. Wallace, M.D.

ABSTRACT **Fifty patients have been operated upon for the tachyarrhythmias associated with Kent bundles. The indications for operation were supraventricular tachycardia (SVT) in 23 and life-threatening tachyarrhythmia in 27. Among the unusual variants noted were multiple Kent bundles in 6 patients and Kent bundles that conducted only retrograde in 3. Forty-nine patients underwent attempted interruption of the bundle of Kent followed by His bundle division in 6. One had elective division of the bundle of His. The surgical problems occurred in 13 patients with posterior septal Kent bundles. A new approach is outlined for this group.**

Division of the Kent bundle was successful in 31 patients, but 2 deaths occurred from cardiomyopathy. Seven patients had successful control of SVT by His bundle interruption. One patient with postoperative retrograde conduction has the SVT controlled with drugs. Eight have postoperative delta waves, but their SVT is controlled with drugs. There were 3 failures.

The surgical technique used in the first successful division of the bundle of Kent for treatment of the tachyarrhythmias associated with Wolff-Parkinson-White syndrome was reported in this journal in 1969 [14]. The success of this and subsequent operations [15, 16] furnished the final proof that the bundle of Kent, an anomalous pathway between the atrium and ventricle, is the cause of this disorder. Its clinical significance rests upon the possibility of its causing a disabling tachycardia or initiating a rhythm that causes sudden death.

The two problems can be explained by two of the properties of Kent bundles (Fig 1). In the first, due to electrophysiological differences that may be present between the Kent pathway and the atrioventricular (AV)–His pathway, a premature atrial or ventricular beat may produce a reentrant supraventricular tachycardia (SVT). The anomalous pathway acts as part of the circuit, most frequently the retrograde portion. Interruption of the His or Kent bundle will break the reentrant circuit. In the second, when the pathway has a short effective refractory period, fast atrial rates such as those associated with atrial fibrillation and flutter can be transmitted to the ventricle unimpeded. Only interruption of the bundle of Kent corrects this problem. Supraventricular tachycardias are unlikely to cause death but may be troublesome and disabling. On the other hand, in patients who have a short refractory period of the anomalous pathway, atrial fibrillation and flutter can result in an intolerable ventricular tachyarrhythmia and death.

The inability to palpate the Kent bundle or to demonstrate it easily has hampered development of a surgical approach to the disorder. The Kent bundles are microscopic in size and may occur in various locations around the right and left annulus fibrosus [3, 7, 8, 10, 11, 13, 19, 20, 22]. It is obvious that the bundle of Kent has to cross from atrium to ventricle; however, the exact route it follows may vary. For example, a pathway may go through the fat pad in the coronary sulcus to the external surface of the ventricular muscle, as we suspected in 1 of our patients, or it may pass from the atrium to the ventricle beneath the endocardium. The ones most difficult to approach surgically course from atrium to ventricle alongside of or in the vicinity of the AV node–His bundle. Whether the pathways are composed of atrial muscle, ventricular muscle, Purkinje fibers, or even nodal tissue is

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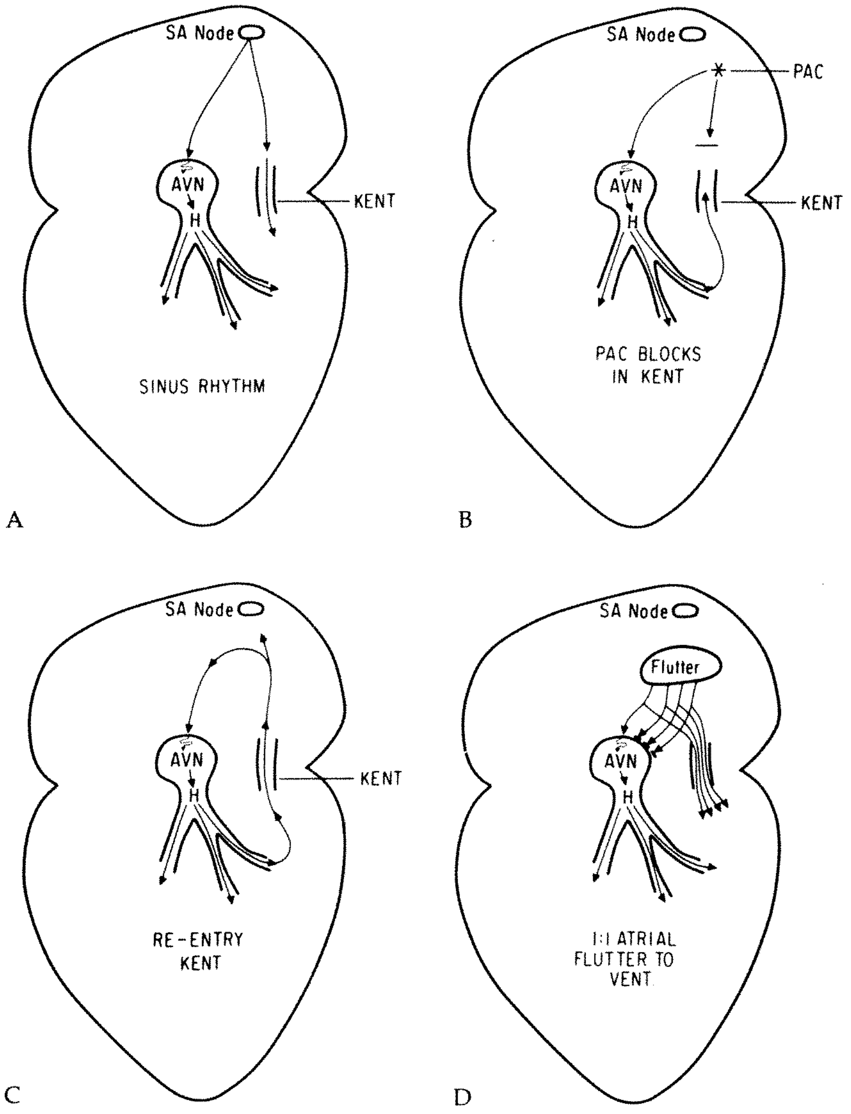


Fig 1. Mechanism of tachyarrhythmias in patients with a Kent bundle. (A) Normal sinus rhythm results in preexcitation, causing a delta wave but with the QRS a fusion one. (B) A premature atrial contraction (PAC) *finds the Kent bundle refractory and the AV node excitable; the impulse goes down the bundle of His, and when the ventricle is reached, the Kent bundle becomes excitable. (C) Retrograde conduction occurs through the Kent bundle to the atrium then back down the AV node, setting up a circus movement and supraventricular tachycardia. Interruption of either the His or the Kent bundle will break the reentry. (D) The problem in a patient who has a Kent pathway with a short refractory period is shown. The AV node normally blocks atrial impulses when they are too frequent, thus protecting the ventricle. The Kent bundle, however, can transmit the impulse to the ventricle 1 : 1. Interruption of the His bundle would not help such a patient.* (AVN = *atrioventricular node;* H = *bundle of His.)*

not known. More confusing yet is the possibility that the pathway might course some distance through the ventricle before making junction with the ventricular muscle. Many of these possibilities are supported by Truex's [19] and Lunel's [10] theories of the role of the annulus fibrosus in eventual separation of the atrium from the ventricle in embryological development.

Two abnormalities that occur in and about the AV node–His area may need to be differentiated from a Kent bundle. These two, although the anatomical evidence of their presence is not abundant, are definite electrophysiological entities, both of which can cause SVT [21]. The first—Mahaim pathways—cause preexcitation, but the P-R interval is usually normal. These pathways arise from just below the AV node and make a junction immediately with the ventricular muscle, bypassing the His-Purkinje system. The second—James pathways—go directly from the atrium to the His bundle, bypassing the AV node. Thus the P-R interval is short, but the morphology of the QRS may not be changed.

The recent advent of practical clinical electrophysiological studies has added to our understanding of the mechanism of the tachyarrhythmias and their life-threatening potential and has permitted precise localization of the conduction pathways before operation [5, 17]. Similar methods are used to determine the site of the Kent bundle at operation as well as to prove that the bundle has been interrupted by the operation. His bundle studies and electrical stimulation of the heart make it possible to determine the following:

1. Proof can be obtained that the short P-R interval and preexcitation of the ventricles are caused by a Kent pathway and not by Mahaim or James fibers.
2. The location of the pathway on the atrioventricular ring can be determined, recorded, and paced by the use of a coronary sinus catheter for the left atrium and a specially designed one for the right atrium. The closer the pacing catheter is to the Kent pathway, the greater the preexcitation. With ventricular pacing or recording during SVT, the atrial activation sequence can be determined, thus locating this end of the pathway.
3. The reentrant SVT conducted along the anomalous pathway can be induced and terminated by properly timed premature stimulation of the atria or ventricles. Thus, using this information and His bundle studies, proof can be obtained that the Kent pathway is involved in the tachycardia.
4. The response of the ventricle to rapid atrial pacing and to induced atrial flutter-fibrillation can be determined, giving an evaluation of the life-threatening potential of the disorder.
5. By means of accurately timed premature stimuli to the atrium and ventricle, the effective antegrade and retrograde refractory periods of the anomalous pathway can be measured, thus providing another assessment of the life-threatening potential of the tachyarrhythmia.
6. Kent pathways that conduct only retrograde, not causing preexcitation of the ventricles but still serving to precipitate a reentrant tachycardia, can be detected.

Since our initial experience, we have observed more than 120 patients with tachyarrhythmias associated with anomalous atrioventricular conduction. From this group, 50 with Kent bundles have been selected for definitive operation while the remainder have been treated with pacemakers and with various antiarrhythmic drugs. This report describes, in the surgically treated group, the indications for operation, the evolution of the operative approach, the results of the procedure, and unusual variations in the clinical picture produced by the bundle of Kent.

Clinical Material

In this report we have included all the surgically treated patients who had a Kent bundle. There were 3 patients who did not have preexcitation of the ventricles because their pathways would only conduct retrograde. Thus, they did not show the typical electrocardiographic changes that are the characteristic of Wolff-Parkinson-

White syndrome. They did have a Kent bundle as a source of the SVT.

The patients represent a select group since their referral to Duke University was for consideration for operation. The selection process was carried still further inasmuch as the surgically treated group represented slightly more than one-third of the patients who were seen by our group. The group operated upon consisted of 11 female and 39 male patients. Their ages at the time of admission varied from 9 to 62 years, with 13 being under the age of 20 years, 20 between the ages of 21 and 40 years, and 13 above the age of 40 years. The onset of their first symptom varied from birth to above the age of 40 years. Thirteen patients began to be aware of irregular heart action before the age of 10 years and 24 from 11 to 20 years of age.

The problems caused by the anomalous pathway that were severe enough to warrant the patient's being considered for operation could be separated into two large categories (Table 1). The first group of patients had recurrent episodes of incapacitating tachycardia. The second group had a life-threatening arrhythmia frequently associated with syncope or documentated ventricular fibrillation. There were 23 patients in the tachycardia group and 27 in the group whose anomalous pathway had the potential for inciting a life-threatening tachyarrhythmia.

In the SVT group, 6 patients gave a history of congestive failure. Four of these had cardiomyopathy and another, acquired mitral stenosis; the sixth, a 19-year-old man who had a retrograde-conducting pathway only, had had intractable tachycardia since birth with rates consistently above 200 beats per minute. The tachycardia group also included 1 patient with severe coronary artery disease and 4 with Ebstein's anomaly. Of the latter 4, 3 had an adequately functioning tricuspid valve while 1 required valve replacement. Four patients had mild syncope unaccompanied by ventricular tachycardia, fibrillation, or an excessively rapid heart rate. Two of the 4 had cardiomyopathy, 1 had sick sinus syndrome, and in the fourth, syncope occurred at the onset of the SVT.

The effective refractory period of the anomalous pathway was measured in 14 of the 23 patients in the SVT group. The determination, expressed in milliseconds, indicates the interval between a regular paced beat and an extra beat that fails to elicit a response in the anomalous pathway. Factors such as the basic pacing rate and the effective refractory period of the atrial and ventricular muscle influence this measurement. The methods used and explanations of the variations are given in a recent publication from this hospital [18]. An effective refractory period below 250 msec is considered short. In only 1 patient was the refractory period below this level, while in the remainder it varied from 270 to 400 msec. During atrial pacing or atrial fibrillation and flutter, the highest ventricular rate noted was 290 per minute in 1 patient. In 8

Table 1. Clinical Findings in 50 Patients with Kent Bundles

Patient Data	Supraventricular Tachycardia (23 pts)	Arrhythmia with Lethal Potential (27 pts)
Above age 31 years	14	7
Syncope	4	20
Sick sinus syndrome	2	0
Cardiomyopathy	4	1
Ebstein's anomaly	4	0
Acquired heart disease	2	0
Ventricular fibrillation	0	12
Ventricular rate over 250 per min	3/12	18/27
Effective refractory period of Kent over 250 msec	10/12	0/8

patients the rate varied between 200 and 250, while in the remaining 12 the highest ventricular rate was below 200 beats per minute.

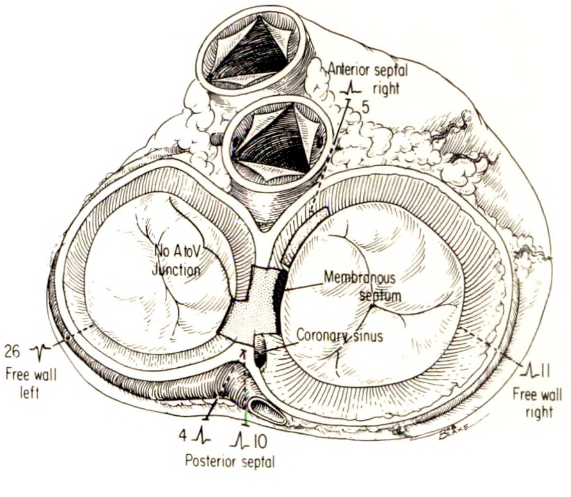
In classifying a patient as having a life-threatening dysrhythmia, one or more of the following points were used: (1) history of ventricular fibrillation or its induction in the electrophysiological laboratory; (2) history of syncope; (3) fast ventricular response to atrial pacing, at rates in excess of 250 beats per minute; (4) fast ventricular response, usually 1:1, to atrial flutter; and (5) the demonstration of a short effective refractory period of the anomalous pathway. There were 27 patients in this group. Twenty of them had a history of syncope that was frequently accompanied by terrifying, life-threatening events. One, a 16-year-old boy, lost consciousness while playing basketball. His father gave him artificial respiration and external cardiac massage for the 25 minutes required to get him to a hospital. He was then resuscitated but for two weeks thereafter was unconscious. He gradually regained his central nervous function and at the time we saw him was in stable condition. Another patient, a 36-year-old woman, was found unconscious in her home by her husband. She was taken to a hospital, where she was found to have ventricular tachycardia that very promptly changed to ventricular fibrillation. Others experienced up to twenty episodes of syncope. It is important to remember that a fast atrial rate in a patient who has a short effective refractory period of his anomalous pathway can be transmitted to the ventricle 1:1, causing the electrocardiographic pattern to resemble that of primary ventricular tachycardia. Twelve had had ventricular fibrillation proved by rhythm strips. In 14 patients the tachyarrhythmia required electrical cardioversion for reinstatement of sinus rhythm.

In the electrophysiological laboratory, the ventricular response to atrial pacing or to induced atrial flutter-fibrillation was determined in 13 patients. In 1 the ventricular response was above 400 beats per minute, in 5 it was from 300 to 400, in 3 from 250 to 300, and in another 3, 200 to 250. In 1 patient the rate was below 200. Four patients developed ventricular fibrillation following initiation of atrial fibrillation.

The effective refractory period of the Kent bundle was measured in 11 patients. Six of them had refractory periods below 250 msec. Three others had periods that were short but were not measurable because of the longer effective refractory period of the atrial and ventricular muscle.

The classification of accessory pathways that we use in this article is based on the findings at operation. Figure 2 indicates the 56 pathways found in our 50 patients. Electrocardiographic changes are helpful in separating the Kent pathways on the right from those on the left but are not always accurate for pathways in the posterior septal area [2, 12]. Instead of continuing to use *type A* for the left and *type B* for the right, we believe the classification of accessory pathways should be changed. *Free wall right* or *left* is used, as shown in Figure 2. The Kent bundles in this location are easily accessible. Twenty-six pa-

Fig 2. View of the heart looking down on the mitral and tricuspid valves. The classification of type A and type B preexcitation, based entirely on electrocardiograms, is not always accurate. The numbers indicate the location of the Kent bundles in our 50 patients; 6 patients had multiple pathways. We now use right *and* left free wall, posterior septal, *and* right anterior septal *to designate pathways. Note that there is no direct connection between atrium and ventricle where the mitral valve is attached to the aorta. The stippled area in the region of the septum indicates possible points where the posterior septal Kent pathways enter the ventricle. In surface mapping, activation in the anterior septal and posterior septal groups shows a "loss of time" between this, the earliest area of ventricular activation, and the onset of the delta wave in the QRS complex. The activation point can be either right or left of the crux.*



tients in our group had Kent bundles on the left free wall and 11 had them on the right free wall. The Kent bundles that cause early ventricular activation on either the right or the left side of the crux are designated *posterior septal;* this group represents unusual surgical problems that are discussed later. Ten of the 14 posterior septal pathways were on the right, 4 on the left. Five patients had anterior septal pathways. These surface on the right ventricle anteriorly but originate at a point anterior to the membranous ventricular septum. They were not difficult to expose and divide at operation.

Three patients had Kent bundles that would not conduct from atrium to ventricle but only in the opposite direction (Table 2). Two, a boy aged 14 years and a woman aged 49, experienced repeated episodes of tachycardia that were refractory to medical management. The third patient, a 19-year-old man, had had a heart rate above 200 per minute all his life and was referred for operation because of repeated bouts of severe congestive failure. Such a pathway can only serve to support reentrant tachycardia.

The occurrence of more than one Kent bundle in a patient had been a theoretical possibility, and in our studies we found 6 such patients. There was a lateral free wall pathway on the left and one on the right in 1 patient. In a second there were two free wall bundles, both on the left side. A third patient had a free wall septal right and a posterior septal right pathway. Another patient had a posterior septal bundle on the right and only a retrograde-conducting pathway on the right free wall. The fifth had two posterior septal pathways, while the sixth had two septal as well as Mahaim and James pathways. This last patient underwent successful division of a septal pathway that was life-threatening; the intact septal pathway, studied two weeks after operation, had a long refractory period and would not support reentrant tachycardia. Two patients were found to have Mahaim fibers plus Kent bundles, and 2 others had James fibers plus Kent bundles.

Table 2. Unusual Variations Noted in 50 Patients with Kent Bundles

Finding	No. of Patients
Retrograde conduction only through Kent bundle	3
Multiple pathways	6
Mahaim pathway	3
James pathway	3
Cardiomyopathy	5
Ebstein's anomaly	4
Sick sinus syndrome	2
Balloon mitral valve	1

Surgical Approach

The surgical procedure for interruption of the Kent bundle consists of two steps: the first is identification of the pathway and the second is its interruption. The heart is exposed through a median sternotomy. Since the anomalous pathways are not visible or palpable, surgical interruption depends upon precise epicardial mapping at the time of operation. However, as our preoperative studies have become more precise and more detailed, electrophysiological studies at operation have served only to confirm the preoperative findings. Now the principal role of surgical mapping is in assessing the results of operation, which includes a further search for other pathways after the dominant one has been interrupted. Both right and left pathways are approached through a median sternotomy. The details of our methods of epicardial mapping, which are adapted and expanded from the methods first developed by Durrer and Roos [4] and Wellens [21], have been described in other publications from this hospital.

The localization of the Kent bundle is done by determining the surface activation sequence of the ventricles and the atria, timing this in milliseconds using a fixed reference point. The atrial and ventricular pacing electrodes are positioned as close as possible to the suspected site of the Kent bundle. A hand-held search electrode is placed at various areas on the surface that correspond to the arbitrary grid map of the epicardial surface. By using both atrial and ventricular pacing as well as mapping during SVT, we have been able to determine the precise area of earliest activation in all our recent patients. Proof that the pathway has been interrupted by the surgical procedure is obtained by repeating the sequence of both atrial and ventricular activation during appropriate pacing, using the same methods employed before division. The check may consist of a preliminary survey while the patient is on bypass, followed by a more detailed study after the heart has been closed.

After the sites of earliest ventricular and atrial activation have been determined, the point on the atrioventricular ring to be divided is approached from within the atrium. It was evident to us before our first operation that it was fundamental for the pathway to be divided just where it crosses the atrioventricular ring. At first, we approached the ring from the epicardial side and divided the ventricle at its insertion into the annulus fibrosus. On the right side this presented very little difficulty, for the right coronary artery could be easily displaced downward; however, on the left, the great coronary vein and coronary sinus caused problems. In addition, injury to the tricuspid valve has much less serious consequences than does injury to the mitral valve. A mild degree of mitral insufficiency was produced in 1 patient by dividing the pathway on the ventricular side of the annulus fibrosus. The Kent bundle is now divided on the atrial side of the annulus. As shown in Figure 3, the fat around the coronary vessels is exposed, then the fat and vessels are dissected away from the top of the external ventricular surface with all bands of tissue, particularly those about the coronary artery and vein branches, being divided.

In the first part of this series, the approach on the left side was by a left lateral thoracotomy. The problems of bleeding and poor exposure of the left atrioventricular ring in a small heart as well as difficulties with coronary veins led us to change this. We now approach the heart through a median sternotomy and expose the left atrioventricular ring in the manner used for exposure in mitral valve replacement. Earlier, because of septal location of tracts in 3 patients, the atrioventricular ring was approached through the atrial septum. The interruption of the Kent bundle is carried out by incising the atrium just above the annulus of the mitral valve, exposing the fat pad that surrounds the coronary artery and vein. If the tract is located anteriorly on the free wall, the incision is begun at the left trigone (anterior insertion of the aorta into the fibrous skeleton of the heart) and carried counterclockwise to beyond the midportion of the annulus of the free wall. If the pathway is on the posterior free wall, the incision is begun at the right trigone (central fibrous body) and extended clockwise to beyond the midportion. In fact, the incisions are now made more and more generous, based on the real possibility that multiple tracts may be present well away from the dominant clinical one. We have had failures in 2 patients with a left free wall pathway; in 1 of them we could not locate the bundle at a second operation. In retrospect we believe the cause was failure on our part to do a complete dissection. Now special care is taken to see that all fat around the coronary vessels is separated completely from the top of the ventricle and annulus, with the dissection carried all the way to the epicardium. This is important because the Kent bundle may be in the fat around the branches of the coronary veins and may even pass underneath the epicardium, though this is not yet proved. Using this approach, we have not injured either the mitral valve or the coronary vessels. The left atrium can be securely closed even

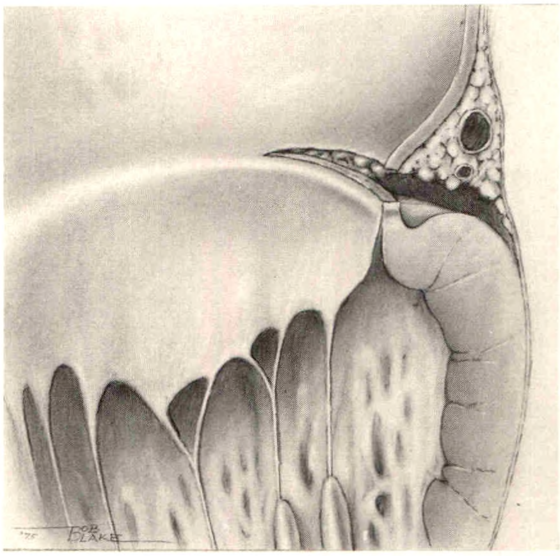


Fig 3. Portion of the interior of the left atrium, showing an incision through the atrial muscle. The fat pad, containing the coronary vessels, is separated from the top of the external wall of the atrium and ventricle all the way to the epicardium. All fibrous bands and even small vessels are divided if they enter the atrium or ventricle. This dissection should be carefully and meticulously done.

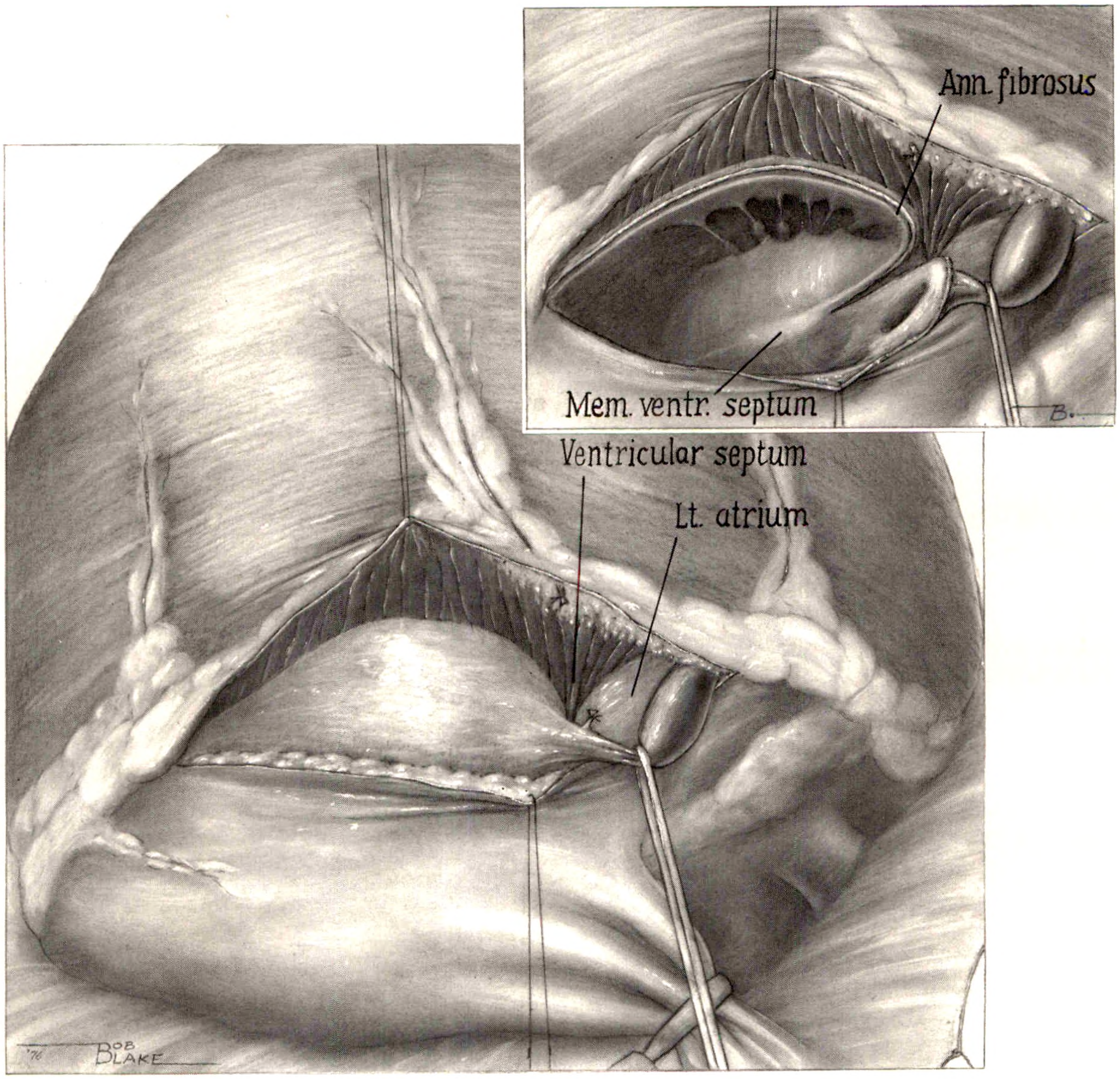


Fig 4. Our current approach for a pathway in the right posterior septal area. The coronary sinus is dissected away from the top of the ventricle after the epicardium has been divided. This exposes a triangular space on top of the ventricular septum that contains the coronary vein and the AV nodal artery, though the latter is rarely seen. The external surface of the right and left atria is also exposed. The inset shows that the incision is through the right atrium and extends almost to the membranous ventricular septum at this level, 2 mm above the annulus. The His bundle is unlikely to be injured because it has already either passed into the membranous septum or entered the ventricle, and here the tricuspid ring is below the mitral one. The left atrium can be entered in a similar way.

though a perforation occurs through the epicardium.

On the right side, our approach to the pathway has been through the atrial endocardium and myocardium with the incisions made just above the annulus fibrosus. In our last 2 patients, however, we have made the incision from endocardium through to epicardium as shown in Figure 4. With this approach it is possible to make an incision from the anterior aspect of the membranous ventricular septum as it protrudes into the right atrium and to carry this all the way around to nearly the same point on the posterior aspect of the membranous septum. As the incision continues toward the membranous septum, there is no more than a slight chance that the His bundle will be injured, for at this level it has entered the membranous septum or joined the left ventricle. In 3 patients in whom we attempted to divide the His bundle by going all the way to the membranous septum, interruption was not accomplished. In the space anterior to the membranous septum there is a fat pad between the external aspect of the right atrial wall and the epicardium even though the coronary artery has not yet entered the coronary sulcus.

One major and as yet not completely resolved problem with surgical interruption of the Kent bundle arose in the 13 patients in whom ventricular activation occurred posteriorly in the region of the crux. This anomaly may be on either the right or the left side of the ventricular septum, usually within 1 cm of the posterior descending coronary artery; by electrophysiological measurement, some of these pathways are on the left and others on the right. The patients usually show a delay in early activation of the ventricle compared with the appearance of the delta wave in the QRS complex, indicating that the impulse has traveled some distance before surfacing. In the free wall pathways, the earliest area of ventricular activation occurs before the delta wave on the electrocardiogram.

In the bundles surfacing to the right of the crux, our approach for dividing the pathway in 2 patients was by elevating the great coronary vein and dissecting it away from the top of the ventricular septum. Then the right atrial endocardium was incised from above the annulus fibrosus, beginning at the anterior lip of the coronary sinus and coursing to the middle of the free wall tricuspid ring. This procedure was successful in both patients. We also approached the Kent bundle through the right atrium, dividing the right atrial wall at the annulus fibrosus as described. We then opened the atrial septum and divided the left annulus fibrosus in a similar manner. Finally, we dissected the great coronary vein away from the ventricular wall. This failed in 2 patients. In a third, in whom it was successful, only the right atrial wall was divided, accompanied by dissection of the fat around the coronary vessels and in the triangular space above the posterior ventricular septum. There was 1 failure with this same technique. In the remaining 3 patients, division of both the right and left atrium at the annulus was unsuccessful. On the left the incision was started at the right trigone, while on the right it began at the anterior lip of the coronary sinus. There were no successes among the 4 patients with early ventricular activation on the left side of the crux, although 2 no longer have tachyarrhythmias. In 1, an incision was made through the entire thickness of the ventricular wall using the approach we first used on the left. A second had division of both the right and left atrium as described.

To sum up our experience and to state our future method of handling these patients, we believe that, first, one should separate the coronary vein completely from the ventricle in the area of the crux. All connections to the muscle at the top of the ventricular septum should be divided. If the earliest area of activation is on the left side of the ventricular septum, then the left atrium should be opened and the annulus divided from the right trigone (central fibrous body) to the lateral midportion of the mitral annulus. If it is on the right side, the right atrium should be divided from the posterior extent of the membranous ventricular septum to the lateral midpoint of the tricuspid annulus.

The methods for division of the His bundle have been by suture ligation either alone or combined with electrocauterization. All require insertion of a demand pacemaker. The procedure, theoretically so easy, turns out to be a difficult one. The details of the surgical approach will be published later.

Results

Results of surgical treatment for this unusual cardiac anomaly have been good (Table 3). The follow-up, with 1 exception, has been complete. With the exception of the 3 deaths, to be discussed later, there have been no major problems beyond the immediate postoperative period. One patient, already mentioned, has a mitral systolic murmur from the ventricular incision that injured the valve. She has no symptoms from this. One patient had injury to the femoral artery that required further care.

In 31 of the 50 patients the accessory pathway was found and successfully interrupted. Two of the patients died, but mapping after interruption of the Kent bundle showed that the division had been accomplished. Postoperatively there has been no evidence of preexcitation in the remainder, and the 29 survivors no longer have tachyarrhythmias. As expected, there has been

Table 3. Results of Operation in 50 Patients with Tachyarrhythmias Caused by a Kent Bundle

Result	No. of Patients	Comment
Kent bundle divided Death due to cardiomyopathy, 2	31	29 asymptomatic
Elective His bundle section; retrograde conduction only	1	Improved, pacemaker (follow-up incomplete)
Delta wave absent; no arrhythmia; antegrade conduction and lethal rhythm abolished His bundle section, 2	3	1 drug control; 2 asymptomatic, pacemaker
Delta wave unchanged; no arrhythmia His bundle section, 4	6	4 asymptomatic, pacemaker; 2 drug control
Delta wave changed; no arrhythmia; Kent bundle damaged Second Kent bundle present, 2 Mahaim pathway, 2	6	4 drug control; 2 with second Kent bundle, no symptoms
Kent bundle missed; failure	3	2 status unchanged; 1 died 18 hr postop, diagnosis questionable

no evidence of regeneration of the bundle, for it is composed of myocardium. In 1 case no attempt was made to find the Kent bundle because of the patient's precarious clinical status; the His bundle was electively interrupted in this patient. In the last 18 patients seen with free wall or anterior septal pathways, operation to interrupt the Kent bundle has been successful.

Six patients still have postoperative electrocardiographic evidence of preexcitation but with a modified delta wave. Two of these patients still have a second posterior septal pathway in spite of the fact that a dominant posterior septal bundle in 1 and a left lateral anomalous pathway in the other were successfully divided at operation. One requires drugs, but both are free of tachycardia. The arrhythmias in the other 4 are controlled with drugs. Two have Mahaim fibers.

In the group of 6 with an unchanged delta wave, 4 had His interruption. Two now have their arrhythmia controlled with drugs.

In 3 patients the Kent bundle was completely missed. One patient died, and if she had a pathway, it was a right anterior septal one. In another there was a right anterior septal pathway. These 2 patients were operated upon early in our experience using the epicardial approach to the ventricle. Their pathways were not accessible with this exposure, since we now believe they entered the ventricle just anterior to the atrial extension of the membranous ventricular septum. The other patient, considered a failure, had Ebstein's anomaly for which she underwent tricuspid valve replacement. She lives at such a great distance from us that we have not been able to get an adequate follow-up evaluation.

Three patients had a pathway postoperatively that conducted only retrograde. Two had His bundle interruption, and the other has the SVT controlled with digitalis.

Three patients died in the immediate postoperative period. The first, a 29-year-old woman, died the night after operation because of uncontrollable tachyarrhythmia. At mapping there was a question whether or not she had an anterior septal pathway. A search for the pathway in the heart at postmortem examination was not successful. The second death was that of a 14-year-old boy who had pathways on the free wall of the right and left ventricles. In spite of extensive studies at our hospital as well as in others, the presence of a severe cardiomyopathy associated with marked concentric ventricular hypertrophy was not recognized. This patient lived for only three days after operation and, in retrospect, was not a candidate for operation. The third death was of a 58-year-old woman who could not be removed from cardiopulmonary bypass. The heart showed extensive fatty deposits throughout. Other than this, we had no explanation for her poor response following operation.

Six of the 7 patients who had His bundle interruption had this done because of failure to divide the Kent bundle. In the seventh patient, a 19-year-old with a retrograde-conducting pathway, His interruption was done electively because of the patient's poor condition. He was in and out of severe congestive heart failure, and the pulse rate had been above 200 all his life. After operation he required pump assistance for 48 hours. He will return for final assessment, for he is improved but still has a heart rate of 120 per minute. Two of the patients, 1 with two left free wall pathways and the second with only one, had residual retrograde function of the Kent bundle. A second attempt to divide the Kent was made in 1 patient. In the second, a 64-year-old man with coronary artery disease, a second attempt to divide the Kent bundle was thought to be too dangerous, and thus His interruption was carried out. Two of the patients, both of whom had interruption of a posterior septal pathway followed by His bundle section, have the anomalous pathway still functioning. The Kent bundle in both patients has the capability of transmitting atrial impulses at a very fast rate, almost 1:1, to the ventricle; therefore, we have not relieved these patients of the possibility of ventricular tachycardia and fibrillation. The remaining 2 are in sinus rhythm by the Kent bundle. All 7 patients have a demand ventricular pacemaker in place.

Certain unusual situations were encountered among these patients. The group with posterior septal pathways has been noted as being the most difficult to treat. Of the 9 patients who had right posterior septal pathways—1 of whom had two—there were 3 successes in the 8 patients in whom an attempt was made to interrupt the pathway (Table 4). Another patient had the anomalous pathway divided, but he now has preexcitation from a Mahaim, James, and probably another septal Kent. The operation failed in the patient already noted who had Ebstein's anomaly. Three had His interruption. Two patients still have their Kent pathway intact but no longer have tachycardia due to change in characteristics of the connection. Four patients had left posterior septal pathways; all Kent pathways were missed. Two of the 4 had His bundle division. The other 2 no longer have tachycardia but still show preexcitation. The group who had potentially lethal arrhythmias contained 11 with posterior septal pathways.

Table 4. Results in Patients with Posterior Septal Kent Bundles

Result	Right Bundle (N = 9)	Left Bundle (N = 4)
Kent bundle divided	3	0
Delta wave, no tachycardia	2	2
His bundle divided	3	2
Failure	1	0

In the earlier part of this experience we were less likely to offer operation to patients in the SVT group with moderately severe symptoms. The results in the group with life-threatening tachycardia show that 17 were cured by Kent division. Seven had function of the Kent bundle disturbed or have a second abnormal pathway remaining that does not have lethal potential. We failed in 3, 2 of whom had to have His section; the latter 2 are, of course, not subject to SVT. In the tachycardia group, 18 had Kent or His division and the 16 survivors are no longer subject to SVT. In 3, the arrhythmia is controlled by drugs. We failed in 2, 1 of whom died shortly after operation.

Of the 3 patients with only retrograde pathways, the bundles in 2 were found and interrupted (Table 5); the other had His bundle interruption and is awaiting postoperative study for final assessment. Cardiomyopathy is frequently found in patients with Wolff-Parkinson-White syndrome. Five patients had this problem. The 2 with right-sided Kent bundles were improved after the pathway was divided, though 1 patient died three years later from progression of the cardiomyopathy. Two of 3 with Kent bundles on the left did not survive. Four patients had Ebstein's anomaly, recognized preoperatively in 2 and discovered at operation in the others. Two patients had a successful operation, 1 did not, and the fourth has a remaining retrograde-conducting pathway that is being controlled with digitalis.

The results in patients with right and left free wall or anterior septal pathways are summarized in Table 6. We have been successful in the last 18 patients with Kent bundles in these locations.

Table 5. Unusual Variations Noted in 50 Patients, Correlated with Operative Results

Variation	Kent Bundle Divided
Retrograde Kent conduction only	2/3
His bundle section, 1	
Multiple Kent bundles	2/5
One Kent remains, 3	
Ebstein's anomaly	2/4
Persistent retrograde conduction, 1	
Failed, 1	
Cardiomyopathy	4/5
Delta wave changed, 1	
Multiple Kent bundles, 1	
Deaths, 2	

Comment

Since the advent of detailed clinical electrophysiological studies of the tachyarrhythmias caused by the bundle of Kent, the complex problems encountered not only in Wolff-Parkinson-White syndrome but in related disorders have been better understood. As a result, these anomalies, once regarded as peculiar electrocardiographic aberrations, are now viewed by clinicians as serious clinical problems with both life-threatening and disabling potential.

Table 6. Results of Operation in Patients with Right Anterior Septal and Right and Left Free Wall Kent Bundles

Result	No. of Patients
Operated upon	37
Kent bundle interrupted	28[a]
Retrograde conduction remains	3
His bundle section, 2	
Drug control, 1	
Delta wave changed	3
Delta wave present; no tachycardia; drug control	1
Failure	2

[a] The last 18 procedures have been successful.

The incidence of sudden death in patients with a Kent bundle is not exactly known. The experience with our patients, highly selected as they were for operation, indicates that the potential for sudden death was present in about one-quarter of the total group and in more than half of the ones operated upon. With our methods of physiological assessment of the anomalous pathways, using the demonstration of a short refractory period and a fast ventricular response to atrial fibrillation and flutter, many of the patients can be singled out who run the risk of sudden death even though their history may not indicate it.

The second criterion for operation, occurring in a little less than half of our patients, was disabling SVT. There were several reasons for advising operation in this group. Some of the patients, because of individual sensitivities, could not tolerate the medication needed for control. There were others in whom the drugs were ineffective even in toxic doses. There was a third group who had some associated problem, such as Ebstein's anomaly, coronary artery disease, mitral valve disease, or cardiomyopathy, that made the episodes of tachycardia difficult to control or to tolerate. A fourth group tended to have more and more problems with tachycardia with advancing age for reasons that cannot be explained. The measurement of "troublesome tachycardia" is not very quantitative, however; and as our experience and confidence in the operation have increased, we have interpreted this term more liberally and have recommended operation for more and more patients in the group with tachycardia alone. A right free wall or right anterior septal pathway can be corrected with a risk, morbidity, and result comparable to or better than that associated with surgical closure of an atrial septal defect. There is a slightly greater operative risk with pathways on the left side; however, we feel as confident in controlling them as with free wall ones on the right.

In the course of our studies on patients with SVT, we have found 3 with an anomalous pathway that conducted only retrograde. The Kent bundle could only cause a reentrant tachycardia. Obviously, these patients did not have preexcitation of the ventricles and thus could not be classed as having Wolff-Parkinson-White syndrome. We found retrograde pathways in addition to but separate from antegrade-conducting ones in 2 patients, and possibly in 2 others. From this experience, the indications for the electrophysiological study are obvious when a patient without preexcitation has SVT that is resistant to treatment.

The basic principle followed in our surgical approach to Kent bundles has been that the pathway should be divided just as it crosses the annulus fibrosus. Formerly, we interrupted the pathway on the ventricular side of the annulus. Now we approach it from the atrial side. The dissection of the fat pad around the coronary vessels is much more extensive now than in the past. Other changes that have evolved with increasing experience have included extending the incision to encompass more and more of the annulus. There is always a possibility that the tracts may be multiple and that some will not be evident until the dominant one causing the electrocardiographic and clinical signs has been divided. Multiple pathways have been found postmortem. By physiological demonstrations they have been found in such locations as the anterior free wall and lateral free wall on the left in 1 patient, and in another, on the left lateral free wall and in the posterior septal area.

The problems in surgical management that have not yet been resolved have occurred in those patients who have anomalous pathways that cause ventricular preexcitation on either side of the crux. Some of them must have pathways that course adjacent to the AV node–His bundle as described by Lunel [10]. However, in 4 of our patients who underwent His bundle interruption, preexcitation continues over the Kent bundle, which of course is against the argument that the Kent bundle lies adjacent to or within the AV node–His system in these patients. The explanation for the other failures is not evident. Some occurred in the early part of our series, and the dissection of the fat pad might not have been extensive enough. There is a time lag in this group between the early area of ventricular activation and the delta wave in the QRS complex, which could mean that the pathway enters the ventricle by way of the septum from either the right or the left atrium. There is a report of a Kent bundle in a dog that had preexcitation from a pathway in the fat around the coronary vessels [1]. This suggests that pathways could possibly go from the atrium and course beneath the epicardium and then around or through the fat in the coronary sulcus before making a junction with the ventricle.

In order to disrupt the circus movement of reentrant tachycardia associated with Kent bundles, interruption of the His bundle would suffice if this were the only consideration. His bundle interruption, even in patients with an antegrade-functioning Kent bundle, calls for a demand pacemaker since the anomalous pathway may not conduct in a reliable manner. One must be careful, except in unusual circumstances, not to change the patient's status from that of being subject to troublesome tachycardia to having his life depend upon an artificial pacemaker. His interruption is only rarely indicated for SVT, such as in 1 of our patients who had elective interruption and in the 2 in whom we failed to divide the Kent completely. When there is only a retrograde-conducting pathway, the patient is entirely dependent upon the artificial pacemaker—the situation of these 3 patients. Patients who have a pathway that conducts atrial fibrillation and flutter to the ventricle at a rapid rate would still be in jeopardy of life-threatening episodes of tachyarrhythmia after His interruption even though reentrant tachycardia is present. Such was the case in 2 of our patients.

The persistence of preexcitation in a patient who no longer has SVT following operation, or in whom SVT is now easily controlled in contrast to the preoperative state, has been noted by Iwa and co-workers [6]. There are several explanations. One is that multiple pathways were present and that once the dominant one was interrupted, the second one became operative but did not have the electrophysiological properties required for supporting a reentrant tachycardia. In other patients the second Kent bundle may be responsive to drugs, whereas the first was not. Another explanation would be that surgical manipulation had partially obtunded the pathway or its connection with the atrium or ventricle. In fact, 1 of our patients did have preexcitation for a year after operation, although he no longer had SVT; finally, as confirmed by electrophysiological study, preexcitation disappeared after this time. The last explanation for persistent preexcitation would be the presence of Mahaim fibers. Similarly, a short P-R interval might be explained by the presence of James fibers. Both problems have been noted in our series.

Our current operative approach to the Kent bundle is cumbersome because of the need to carry out surface mapping in order to locate the pathway. This is further compounded by the repeat preliminary mapping that must be done while the patient is on cardiopulmonary bypass in order to determine the success of the interruption and to prove that no other pathways are present. As our preoperative studies have become more detailed, we have been successful in locating the pathway before operation. The postoperative epicardial mapping and pacing studies have been the most useful part of the intraoperative study, preventing us from terminating the procedure before the Kent bundle has been interrupted. In the posterior septal pathways in particular, failure to obliterate the anomalous pathway has led us to go ahead with His bundle interruption at the same operative procedure. In the present state of our knowledge, there seems to be no way of avoiding these detailed studies at operation, as tempting as it may be to accept the preoperative ones and then go ahead with a wide incision of the atrium above the annulus fibrosus on the appropriate side.

The surgical treatment of the tachyarrhythmias that accompany anomalous pathways of atrioventricular conduction is now well established as a safe and curative operation. Since the SVT in these patients represents the classic example of reentrant tachycardia, this could serve as a model on which we can base extension of the surgical principles outlined here to other reentrant SVTs. If this is done, it will require the same precise electrophysiological localization of the reentrant site, followed by an operative procedure to interrupt the reentry that preserves all or some of the supraventricular control of the heart rate.

Addendum

Since we submitted this article for publication, 18 additional patients have had successful Kent bundle interruptions. These were done in succession.

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Clinical and Hemodynamic Performance of a Totally Flexible Prosthetic Ring for Atrioventricular Valve Reconstruction

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ABSTRACT **A new, totally flexible ring for atrioventricular annuloplasty is described. The technique for its insertion closely follows the principles of Carpentier's selective annulus reconstruction [4]. Ninety-nine such rings have been inserted (47 in the mitral and 52 in the tricuspid position); 45 valves were simultaneously replaced. There were 6 (4 hospital and 2 late) deaths. The thromboembolic incidence was 4.8%. No instances of dehiscence or late ring deterioration have been detected. Thirty-four patients have been recatheterized, 19 of them with mitral rings. The mitral gradients and angiographic findings show the correct functioning of the implanted ring. It is concluded that use of this flexible ring, which adapts to the continuous changes of the normal mitral annulus, produces a more physiological type of valve operation.**

Our clinical experience with more than 150 Carpentier ring annuloplasties [7] led us to develop a new, totally flexible prosthetic ring that can be used for both the mitral and the tricuspid valve. It was thought that a flexible ring would conform more physiologically to the continuous changes in the atrioventricular annulus during the cardiac cycle, thus decreasing the chances of partial detachment and interfering less with normal ventricular kinetics. The clinical experience with this ring, particularly when used in the mitral area, forms the basis of this communication.

The Flexible Ring

The 3 mm thick, circular ring is made of Dacron velour. It can adopt any configuration and can be deformed in any plane (Fig 1). Due to its elasticity, it can increase its circumference by 10%. A radiopaque thread makes it visible on roentgenograms. The rings are made in circumferences of 78, 84, 90, 96, and 102 mm. They are marked at three equidistant points that serve to identify the individual ring as being of size 26, 28, 30, 32, or 34.

A similar operative technique has been used in all patients. Total-hemodilution extracorporeal circulation with moderate total-body hypothermia (30°C) has been used along with a standard midline incision. Uninterrupted aortic cross-clamping with local hypothermia was the sole method of myocardial protection.

Once the decision to place a ring is made, the technique for its insertion follows closely the principles described by Carpentier and associates [4]. With practice, placement should not take more than 15 to 20 minutes.

Clinical Material

Between January and December, 1975, 99 flexible rings were placed in 83 patients. There were 16 men and 67 women with an age range between 15 and 63 years (mean, 40). Twenty-five patients had mitral and 58 had polyvalvular disease. Forty-seven rings were placed in the mitral position with 8 insufficient, 9 stenotic, and 30 mixed lesions. For the tricuspid valve, 52 rings were used on 37 functional and 15 organic tricuspid valve lesions. Among the 83 patients, 45 had valves simultaneously replaced with 43 Hancock xenografts and 2 Björk-Shiley prostheses (31 mitral and 14 aortic). Fourteen aortic valvuloplasties and 1 simple mitral commissurotomy were also performed, making a total of 159 valves treated operatively in this group of 83 patients (Table 1). No anticoagulants were used except when a giant left atrium was present. No patient has been lost to follow-up so far.

Right and left catheterization plus left cinean-

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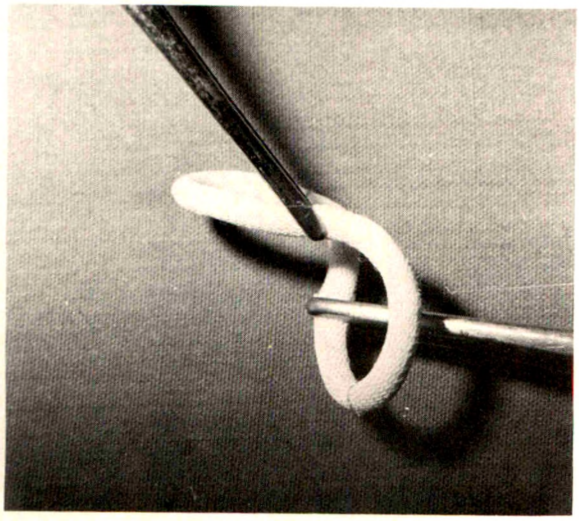

Fig 1. The flexible atrioventricular ring under torsion stress to show its flexibility.

giography were routinely performed in all patients before operation and in 34 patients postoperatively. The mitral valve elasticity index* was also calculated. In a small group of 12 patients the percentage of circumferential shortening of the basal area of the left ventricle was calculated on the left ventricular angiograms before and after operation [7] and compared with 7 Carpentier rings and 11 Hancock xenografts.

Results

In this group of 83 patients there has been a total of 6 deaths (7.1%), 4 of which occurred in the hospital and 2 at a later date (see Table 1). All 6 patients had both mitral and tricuspid lesions, and among them they received 3 mitral Hancock valves, 1 mitral Carpentier ring, 2 mitral flexible rings, and 6 tricuspid flexible rings. The hospital deaths were due to hemorrhage (1), pulmonary embolism (1), and low cardiac output (2). One of the patients who died in the hospital was on intraaortic balloon pumping for 12 days before death. The 2 late deaths were due to cerebral hemorrhage and a documented myocardial infarction, respectively.

No ring dehiscences have occurred so far. One patient had to undergo reoperation after 11 days to replace the mitral valve by a prosthesis. The patient had congenital mitral insufficiency, and in the postoperative period no murmur had been detected. Ten days afterward, a loud systolic murmur appeared. Recatheterization showed massive mitral insufficiency, and at operation it was found to be due to elongation of the chordae tendineae.

There have been 4 nonfatal thromboembolic phenomena in the whole series (4.8%). All except 1 patient recovered completely without sequelae. Two patients had a Hancock mitral bioprosthesis (1 of whom had a peripheral and a central embolus), and 2 patients had a flexible mitral ring. Both of these patients were taking dipyridamole, and 1 of them was in sinus rhythm. Postoperatively 20 patients with flexible mitral rings had an apical systolic murmur (44%); 10 had a grade 1/6, 8 a grade 2/6, and 2 a grade 3/6 murmur. One of these last patients is the 1 described with congenital mitral insufficiency. Thirteen patients had a diastolic murmur (28%), while 12 patients (26%) had no mitral murmurs. All patients with flexible mitral rings improved postoperatively to NYHA Functional Class I or II except 1 (Fig 2). The clinical and hemodynamic results with the tricuspid rings will be reported elsewhere.

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*Ochoteco A, Ubago JLM, Colman T, et al: Mitral valve distensibility: a hemodynamic and cineventriculographic assessment. Submitted for publication.

Table 1. Clinical Experience with Flexible Ring for Atrioventricular Annuloplasty

Type of Lesion	No. of Patients	Mortality		
		Hospital	Late	Total
Mitral	25	0	0	0
Mitral & tricuspid	32	4 (12.5%)	2 (6.25%)	6 (18.7%)
Mitral & aortic	5	0	0	0
Mitral, aortic, & tricuspid	21	0	0	0
Total	83	4.8%	2.4%	7.2%

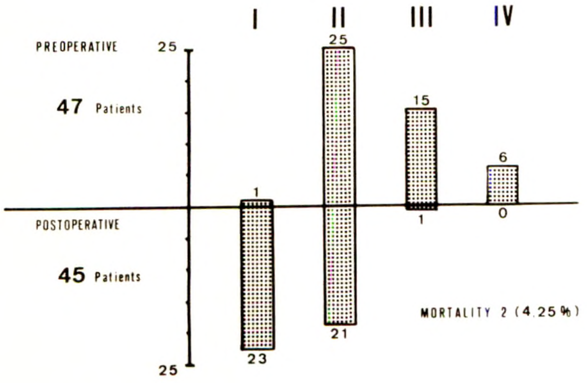


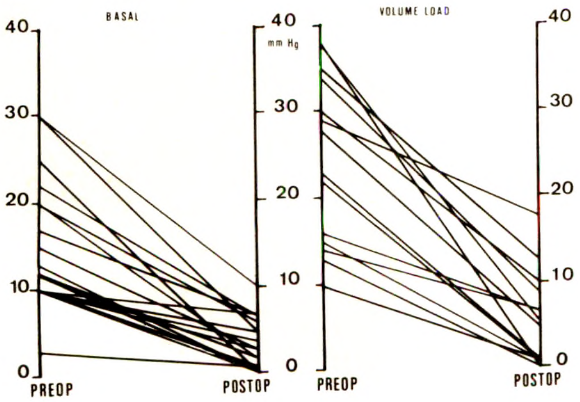
Fig 2. *NYHA Functional Class before and after placement of flexible atrioventricular rings in the mitral position.*

Hemodynamic Results

In all but 1 of the patients with a flexible mitral ring who were recatheterized, the basal simultaneous middiastolic transmitral gradients decreased to a maximum of 7 mm Hg. In the 1 patient with mixed mitral disease with predominant insufficiency, a large (No. 32) ring was placed, achieving perfect valve closure that was checked at the time of operation and by angiography. Following volume loading, the transmitral gradients were all below 12 mm Hg except in the patient with congenital mitral insufficiency (Fig 3). The pulmonary resistances decreased, particularly venous resistance, as could be expected (Fig 4).

Angiographically we have classified the amount of mitral insufficiency as grade 1 when a regurgitant jet is just seen, without filling the atrium; grade 2 when it fills the atrium after a few systoles; and grade 3 when it fills the atrium in the first systole (Fig 5). Only 4 patients had mitral insufficiency, 2 of whom had grade 1 insufficiency and had no abnormal left atrial pressure tracings. One of the patients with grade 3 insufficiency was the patient with congenital mitral insufficiency.

Fig 3. *Simultaneous transmitral gradients before and after placement of flexible atrioventricular rings.*



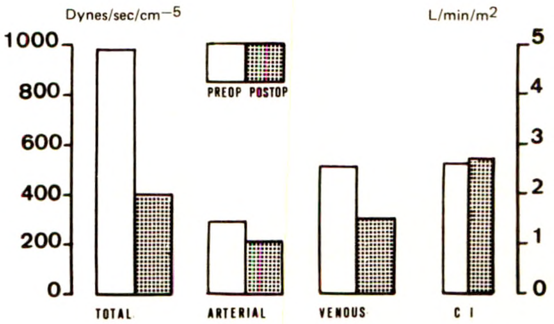


Fig 4. *Pulmonary resistance and cardiac index before and after flexible mitral ring annuloplasty.*

The hemodynamic data in 30 patients with correctly placed flexible rings (12), Carpentier's rings (7), and mounted xenografts (11) were compared in order to determine whether there was any detectable difference between the groups (Table 2). All 30 patients had no statistically significant difference in their ventricular function (ejection fraction and volumes) or in their intrinsic left ventricular contractility. No differences could be found between the basal diastolic gradients in the three groups of patients. After volume loading there was no difference between the two ring annuloplasties, but a residual gradient was found in the group with xenografts. Comparing the preoperative and postoperative angiograms, the patients with

Fig 5. *Summary of cineangiographic findings before and after flexible ring annuloplasty. Mitral insufficiency, grade 1 = regurgitant jet just seen, without filling the atrium; grade 2 = jet fills the atrium after a few systoles; grade 3 = jet fills the atrium in the first systole.*

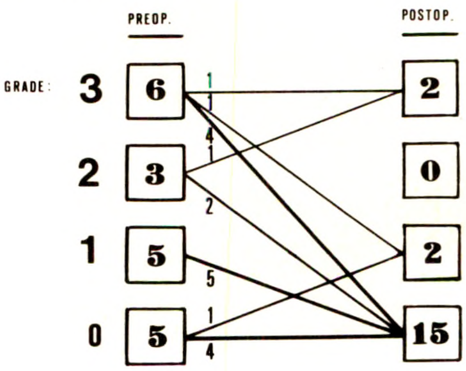


Table 2. Mitral Hemodynamic Data in 30 Patients with Correctly Placed Atrioventricular Flexible Rings, Carpentier Rings, or Mounted Xenografts

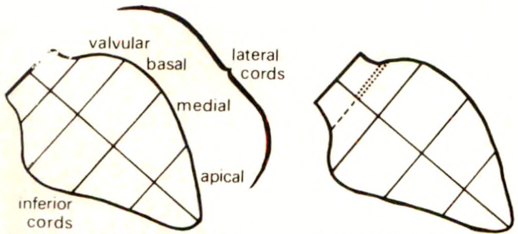
Hemodynamic Measurement	Flexible Ring (12 patients)		Carpentier Ring (7 patients)		Hancock Prosthesis (11 patients)	
	Preop	Postop	Preop	Postop	Preop	Postop
V_{max} (circ/sec)	1.7 ± 0.6	2.1 ± 0.6	1.9 ± 0.3	2.2 ± 0.6	1.4 ± 0.3	1.5 ± 0.3
Ejection fraction (%)	58 ± 7	58 ± 7	65 ± 3	64 ± 4	58 ± 7	56 ± 6
Transmitral gradient						
Basal	15 ± 8	4 ± 3	12 ± 8	3 ± 2	17 ± 8	6 ± 3
Volume load	24 ±10	6 ± 5	16 ± 8	14 ± 3	21 ± 12	13 ± 10

flexible rings showed a significant increase in their systolic shortening of the basal area of the left ventricle, particularly of its diaphragmatic inferior aspect, while in the patients with rigid structures (Carpentier rings and mounted xenografts), the improvement was localized to the anterior or lateral aspect of the basal portion (Fig 6).

Comment

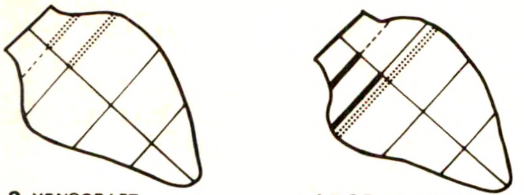
In spite of continuous improvements in their design and construction, prosthetic heart valves are still plagued by a host of problems which result in patients selected for operation being restricted to those with a very serious clinical and hemodynamic impairment. The indications for operation are only widened when it is thought that a simple commissurotomy will solve the problem. This situation, however, ignores the progressive and irreversible damage inflicted upon the myocardium subjected to long-standing hemodynamic stress. The argument for early operation needs to be backed by a simple, safe, and stable type of conservative procedure. So far only the atrioventricular valves seem amenable to this type of operative approach. Since the early attempts of Lillehei and associates [12], a number of procedures have been described and abandoned [1–3, 8, 14, 15]. The best results were achieved with the technique of posteromedial annuloplasty described by Merendino [13] and improved by Kay [11], Wooler [19], and Reed [16] and their coworkers. Carpentier and his associates [4], by describing a selective ring remodeling technique which makes the most of the available leaflet tissue, have rehabilitated the valvuloplasties. It has been shown that the technique gives long-term, stable results [9, 10], and our very satisfactory personal experience with more than 150 Carpentier rings has shown us its reproducibility [7].

Fig 6. Diagrams of left ventricular cineangiograms divided by cords perpendicular to the longitudinal axis. The systolic circumferential wall shortening has been calculated preoperatively and postoperatively in each group. Dotted lines *indicate increased percentage of postoperative wall shortening.* Thick lines *indicate a statistically significant ($p < 0.05$) improvement.*



1. LEFT VENTRICULOGRAM

2. CARPENTIER RING



3. XENOGRAFT

4. DCP FLEXIBLE RING

The experimental work of Tsakiris and colleagues [17, 18], which clearly showed the continuous changes of the normal mitral and tricuspid annulus during the cardiac cycle, made us consider the possibility of constructing a totally flexible ring for atrioventricular annuloplasty. We thought that such a ring would accommodate and follow the movements of the annulus and at least decrease its chances of becoming partially detached, reducing the stress forces on any particular point. As far as we know, Carpentier has worked experimentally on a semiflexible, constant-shape ring [5], but ours is totally flexible and will follow the stress forces exerted on it. Applying the operative principles of Carpentier for selective valve reconstruction, we found that the flexible ring, which at the time of its insertion takes any form, adopts a configuration extremely similar to a Carpentier rigid ring once it is in place and has been subjected to systolic work. The physiological systolic reduction of the mitral annulus is not impaired by a totally flexible ring, and therefore better valve closure should theoretically be achieved. In the tricuspid area, this technique occupies a place between Carpentier's rigid ring and De Vega's semicircular annuloplasty [6].

Our clinical results seem to parallel those with the rigid ring and to support its superiority to a prosthesis. We believe that the high number of systolic murmurs (44%), which includes all the early systolic ones, is not very significant. Those patients who were recatheterized (and all doubtful cases were obviously restudied) showed, both hemodynamically and angiographically, only 2 instances of significant mitral insufficiency. The diastolic murmurs (27%) must correspond to the small transmitral gradients, and they are also found in patients with a Hancock prosthesis. Hemodynamic comparison between the flexible and the rigid ring shows that there is no difference in their transmitral gradients. A significant difference, however, has been found in the gradients between the annuloplasties and the Hancock bioprosthesis after volume loading. Study of systolic left ventricular wall motion has shown that postoperative improvement in ventricular movement is more marked when a flexible ring rather than a rigid structure has been placed in the mitral annulus.

It is obviously still too early to consider this technique established. If it does become standard, however, it will considerably enlarge the indications for operation at an earlier stage of valve disease.

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Discussion

DR. AGUSTIN ARBULU (Detroit, MI): I greatly enjoyed the paper by Dr. Duran. I think that the concept of using a flexible ring in the atrioventricular position as a method of reconstructing the mitral or tricuspid valve is interesting. I would like to ask Dr. Duran two questions. First, since he reports the development of nonsignificant systolic murmurs in 43% of his patients, I would like to know if, in the late follow-up of these individuals, these murmurs have changed or if the mitral or tricuspid insufficiency has become significant? Second, the comparative study with the rigid Carpentier ring, at least in my interpretation, indicates no difference between the rigid and the flexible ring. I would like to know if this similarity continues during the progress of these patients?

DR. FERNANDO ALONSO-LEJ (Oviedo, Spain): I have been interested in the operative treatment of advanced cases with organic tricuspid insufficiency using a modified De Vega annuloplasty. The sutures are placed from the outside to the inside on the tricuspid annulus while the cardiopulmonary bypass period is being completed. After the right atriotomy is closed, the sutures are passed through a Dacron pledget. The patient is removed from cardiopulmonary bypass prior to performance of the annuloplasty; the annuloplasty is done with the patient off cardiopulmonary bypass by tying the previously placed annular suture until the V wave of the right atrial recording disappears.

In a 73-year-old woman who underwent this reconstruction we obtained simultaneous recordings of the right atrium and ventricle through previously placed catheters. The V wave of the right atrium indicated ventricularization of this chamber by the regurgitant flow. The V wave was completely eliminated in the right atrium when the heart was contracting once cardiopulmonary bypass was discontinued after the annuloplasty. The tricuspid insufficiency was corrected, and we had an objective physiological measurement.

In our smaller series of 8 patients operated upon in the past 5 years, we have had no complications or thromboembolic problems; this is the type of annuloplasty that I prefer.

DR. ALAIN CARPENTIER (Paris, France): I would like to congratulate Dr. Duran for his continuing interest in prosthetic ring valvuloplasty. We also have been interested in investigating flexible rings. As Dr. Duran showed, it is a little bit disappointing to see that, contrary to what one could expect, there was no significant difference in the performance of flexible and rigid rings except for the shortening of the basal portion of the ventricle, the value of which remains to be proved.

Experimentally, Turina and Senning from Zurich inserted prosthetic rings in dogs and found no difference in ventricular function in comparison with their control group as long as 15 months afterward. The main importance of the flexible ring is to reduce the stress on the suture line during systole. But this flexibility has to be selective in order not to impair the remodeling of the annulus, which is a fundamental objective of the ring valvuloplasty. I myself am reluctant to use a completely flexible ring which acts as a simple circular strip of Dacron.

I would like to point out that the ring valvuloplasty is only a part of mitral valve reconstruction. Associated lesions must be treated as well to achieve a perfect result. Elongation of chordae tendineae, for example, is present in 20% of patients with pure mitral insufficiency and must be treated by either wedge resection, shortening of the chordae, or sliding plasty of the papillary muscle. In combined mitral stenosis and insufficiency, the leaflets can be thinned and mobilized by resection of hypertrophic secondary chordae.

We now have more than 500 cases of mitral valve reconstruction at Broussais Hospital in Paris. The results in the first 320 patients show a low incidence of reoperation and a thromboembolic episode rate of 0.8%, despite the fact that anticoagulation was discontinued after 1 month in 69% of the patients. The actuarial curve showed 90% survival at 6 years.

DR. DURAN: Thank you very much for your comments. In connection with the insufficiency murmurs, the rate of 44% is high, but it includes every single small, early systolic murmur detected by the cardiologists who follow our patients.

In fact, as you saw, angiographically only 4 patients showed a regurgitant jet, 2 of which had no hemodynamic significance. We have no evidence of a change in the murmurs, which were all present from the moment of operation and therefore are not due to ring deterioration.

The question about the difference between the Carpentier ring and our flexible ring is very pertinent. We did not find any detectable difference in terms of gradients, either basal or after volume loading. The only difference was in the movement of the left ventricular wall, which in our opinion showed that the flexible ring is more physiological.

Finally, with regard to the question about whether a strip of Dacron would function the same as a flexible ring, I do not think so, because the success of this technique is based on the principles of Carpentier annuloplasty. One does not place the sutures to reduce the mitral annulus indiscriminately, but rather in such a way that one makes the most of available leaflet tissue.

Surgical Treatment of Acute Aortic Regurgitation in Infective Endocarditis

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James D. O'Toole, M.D., James A. Shaver, M.D., and Henry T. Bahnson, M.D.

ABSTRACT **During a six-year period 15 consecutive patients with isolated aortic regurgitation due to infective endocarditis were encountered. None had prior significant aortic valve disease. Elective valve replacement was performed in 13 patients; emergency operation was needed in only 1 patient because of intractable pulmonary edema. One patient died suddenly from acute heart block while undergoing medical treatment.**

Preoperative cardiac catheterization studies in 10 of the 14 patients revealed gross elevations of left ventricular end-diastolic pressure, pulmonary hypertension, depressed cardiac output, and 3 to 4+ aortic regurgitation. There was 1 early and 1 late postoperative death, both due to systemic embolism, yielding an overall surgical mortality of 14%. After a mean follow-up of 18 months, 10 of the 11 patients are in New York Heart Association Functional Class I.

Most patients with acute aortic regurgitation secondary to infective endocarditis have clinically observable congestive heart failure and will eventually require valve replacement. If congestive heart failure can be stabilized by a medical regimen, a course of antibiotic therapy can be administered and elective valve replacement can be performed. The time taken for preoperative antibiotic treatment is not associated with irreversible myocardial damage sufficient to influence the results of operation.

Infective endocarditis of the aortic valve is a major cause of acute aortic regurgitation [3]. When this valvular lesion occurs in patients with normal left ventricular compliance, a clinical and hemodynamic picture is produced which contrasts sharply with chronic aortic insufficiency [18, 23]. Therefore, the management of aortic insufficiency occurring in infective endocarditis may differ depending upon the presence or absence of prior significant regurgitation. Although several authors [2, 5–7, 15, 22, 25] have recommended urgent valve replacement for the acute lesion, the timing of operation in patients other than those with severe unresponsive congestive heart failure remains unclear. The purpose of this report is to relate our experience with 15 consecutive patients manifesting the syndrome of acute aortic regurgitation.

Clinical Material

Between August, 1968, and October, 1974, 15 patients with acute aortic insufficiency resulting from infective endocarditis were seen at Presbyterian–University Hospital and the Veterans Administration Hospital of Pittsburgh. All patients with endocarditis at these institutions were seen by one or more members of the University Cardiology Service. The infective organism was isolated from blood cultures in all but 1 patient. Medical management of infection and congestive heart failure was attempted in all patients. Symptomatic congestive heart failure was categorized according to the New York Heart Association Functional Classification. Of the 15 patients, 10 underwent right heart and retrograde or transseptal left heart catheterization; the left ventricle was entered in 8. Aortic root angiography was performed in all 10. Fourteen of the 15 patients underwent aortic valve replacement. Ten of these patients have been followed for a period varying from one month to four years. Postoperative catheterization was performed in 2 patients two and three years following operation, respectively.

Ten patients were known not to have a

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preexisting murmur of aortic regurgitation based upon prior medical examination. Of the remaining 5, 2 had hemodynamically insignificant disease of the aortic valve manifested by a basal systolic murmur. No prior data were available on 1 patient, and 1 had no roentgenological evidence of cardiac enlargement or electrocardiographic manifestation of left ventricular hypertrophy. The fifth patient manifested a cardiothoracic ratio of 55% three and one-half months after the onset of bacterial endocarditis but had no electrocardiographic evidence of left ventricular hypertrophy. In summary, of the 15 patients, 10 had no evidence of preexisting aortic regurgitation and 4 probably had no significant valvular disease prior to infection. Two of the 15 patients had mitral regurgitation murmurs. The murmur was audible in only 1 patient prior to the onset of endocarditis.

The infecting organism was isolated from blood cultures in 14 of the 15 patients (see Table 1). One patient in whom blood cultures were negative had been treated with antibiotics for a long time for supposed bronchitis. However, one positive blood culture had been obtained in this patient in another hospital before he was transferred to our care. The duration of antibiotic therapy varied from a minimum of four weeks to a maximum of twelve weeks (see Table 2). All patients had persistently negative blood cultures prior to operation.

Clinical Features

Clinical data on the patients are summarized in Table 1. At the time the patients were seen at Presbyterian–University Hospital and Veterans Administration Hospital 7 were in Functional Class III and 7 were in Class IV. The only patient

Table 1. Clinical Features of 15 Patients with Aortic Regurgitation due to Infective Endocarditis

Patient & Age	Infecting Organism	Duration of Treatment[a] (wk)	Total Duration of Illness[b] (mo)	NYHA Functional Class Before Operation	NYHA Functional Class After Operation	Embolism	Comment
C. R., 23	Beta-hemolytic streptococcus	9	4	III	. . .	Postoperative	Died of coronary embolism 3 wk postop
J. C., 55	Enterococcus	12	4	IV	I	. . .	. . .
R. C., 53	. . .	4	9	IV	II–III	. . .	Continued LV dysfunction
L. D., 54	*S. viridans*	4	2	IV	I	. . .	. . .
A. D., 17	*S. viridans*	3	2	III	I	Left femoral & splenic arteries	. . .
C. G., 68	Alpha-hemolytic streptococcus	8	2	IV	I	. . .	. . .
L. G., 63	Enterococcus	6	1 1/2	IV	. . .	. . .	Died 7 wk postop
W. R., 63	Beta-hemolytic streptococcus	4	1	IV	I	Cerebral	. . .
L. W., 20	*S. aureus*	4	3 1/2	IV	I	Right femoral artery; mycotic aneurysm	. . .
J. Y., 53	*S. aureus*	8	2	III	I	. . .	. . .
J. W., 31	*Candida tropicalis*	1	1	II	. . .	Left femoral	. . .
T. P., 52	*S. viridans*	1	3	III	. . .	. . .	Died preop, acute heart block
A. F., 51	*S. viridans*	6	5	III	I	Cerebral	. . .
D. L., 26	*S. viridans*	6	6	III	I	. . .	. . .
J. F., 52	*S. bovis*	5	4	III	. . .	. . .	. . .

[a] Duration of antibiotic therapy before operation or death.

[b] Duration of illness as judged from first medical attention to death or operation.

LV = left ventricle.

in Class II had fungal endocarditis. Digitalis and diuretics were administered to all patients. Stabilization of congestive heart failure was achieved to the point that the patients were asymptomatic at bed rest. Clinically evident arterial embolic episodes occurred in 4 patients with bacterial endocarditis. Only 1 had multiple episodes. The embolism sites included two in the cerebral, three in the femoral, and one in the splenic artery. All patients manifesting systemic embolism were in congestive heart failure.

Hemodynamic Data

Ten patients underwent cardiac catheterization prior to operation. Hemodynamic data are summarized in Table 2. All patients had severe aortic regurgitation documented by angiography. Mitral valve regurgitation was present in 2 but was significant only in 1. Marked pulmonary hypertension (mean pulmonary artery pressure of 30 mm Hg or more) was present in 8. Left ventricular end-diastolic pressure (LVEDP) varied from 30 to 60 mm Hg. Aortic diastolic pressure tended to equal LVEDP. Of 8 patients in whom these two variables were measured, the difference was less than 20mm Hg in 5. Cardiac index was less than 2.4 L/min/m^2 in 7 of 9 patients.

Case Reports

The following case reports emphasize specific points gained from our experience in the management of acute aortic regurgitation due to infective endocarditis.

Patient 1

J. Y., a 53-year-old man, was admitted with pneumonia complicated by pericarditis with effusion. Pericardial fluid as well as blood cultures yielded coagulase-positive *Staphylococcus aureus*. Fifteen days later he developed congestive heart failure, and a murmur of aortic regurgitation was heard. He was treated with antibiotics, digitalis, and diuretics. He was asymptomatic at bed rest, permitting discharge after eight weeks, but he developed dyspnea on mild exertion that necessitated readmission for cardiac catheterization, the results of which are shown in Table 2. He underwent elective valve replacement, and at operation a large tear was seen in the right leaflet extending to the noncoronary leaflet. Recovery was uneventful. Two years later a restudy showed normal hemodynamics. Five years after the operation the patient remains asymptomatic.

This patient's history illustrates that congestive heart failure secondary to acute aortic regurgitation can be stabilized to allow full antibiotic therapy, with elective valve replacement resulting in a favorable outcome. The preoperative chest roentgenogram showed moderate cardiomegaly (Fig 1A), whereas the heart size was normal four months after operation (Fig 1B).

Table 2. Hemodynamic Data in 10 Patients with Aortic Regurgitation due to Infective Endocarditis

	Pressures (mm Hg)							
		LA						
Patient	PA Mean	Avg	Mean	LVED	Aortic Diastolic	Cardiac Index (L/min/m^2)	Aortic Regurgitation	Mitral Regurgitation
J. C.	65	45	35	45	45	1.41	4+	2+
R. C.	50	40	28	60	60	1.31	4+	...
L. D.	20	...	...	34	55	3.54	4+	...
G. G.	26	30	23	...	40	...	4+	...
L. G.	40	28	22	32	40	2.14	4+	...
L. W.	50	35	32	...	60	1.16	4+	1+
J. Y.	30	38	24	30	80	2.37	3+	...
A. F.	55	55	40	40	40	1.75	4+	...
D. L.	32	36	...	35	80	2.27	4+	...
J. F.	35	25	...	30	50	3.65	4+	...

LA = left atrium; LVED = left ventricular end-diastole; PA = pulmonary artery.

Patient 2

C. R., a 23-year-old man, was known to have congenital aortic stenosis but was asymptomatic. Two months after a dental procedure he developed bacterial endocarditis, and beta-hemolytic streptococcus was isolated on blood cultures. He was treated with penicillin and streptomycin for nine weeks, but he developed congestive heart failure that was only moderately controlled with medical therapy. Because of continued symptoms, he underwent aortic valve replacement.

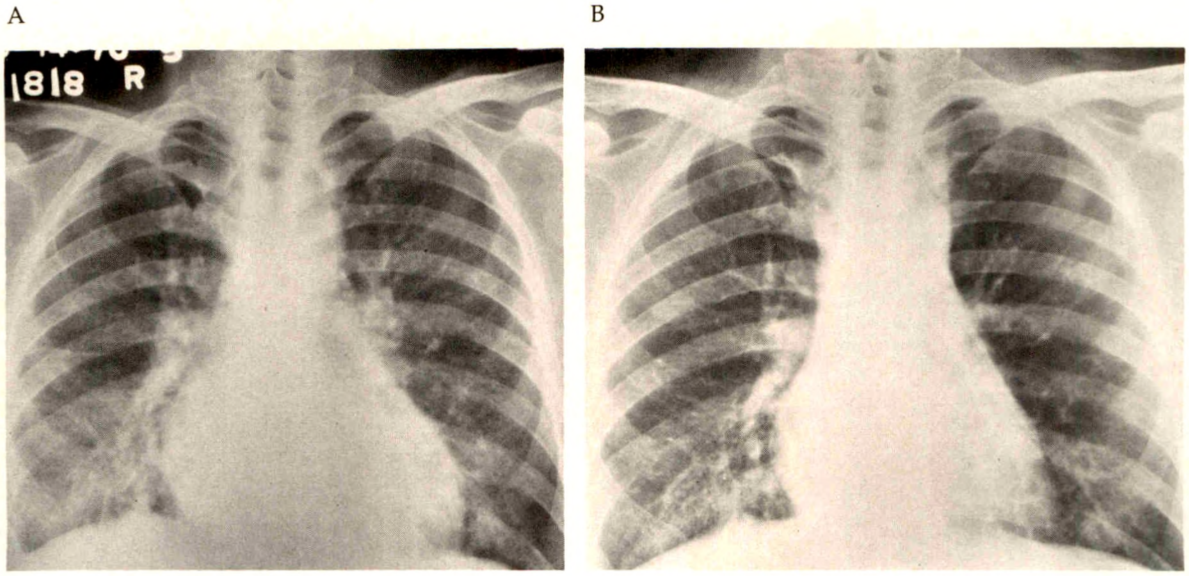
At operation the valve was found to be bicuspid with a rudimentary commissure between the right and left leaflets. Considerable prolapse of the combined leaflets with rolling of the edges was noted. There was a perforation in the midportion of the left leaflet, which was the only one grossly involved with endocarditis. At the base of the leaflet, near the perforation, was an additional hole that communicated with the ventricle. This hole seemed to be an abscess that had ruptured, since it involved the ring rather than the tissue of the leaflet. Friable vegetation was present in the region of the perforation, and similar small bits of vegetation extended down to the mitral valve.

The patient made an uneventful recovery from operation, but three weeks later he developed sudden chest pain and died. Postmortem examination disclosed a massively enlarged heart weighing 760 gm. The left anterior descending and circumflex coronary arteries were large and widely patent. However, the right coronary artery was extremely small and could not be followed for more than about 2 cm. There was both macroscopical and microscopical evidence of acute infarction of the posterior wall and focal embolic scarring. There were several small, firm fibrotic pieces of vegetation below the aortic valve and a jet lesion adjacent to the mitral valve. This was the only death probably due to coronary embolism in the series, and it occurred three weeks postoperatively.

Patient 3

R. C., a 53-year-old man, had been treated with antibiotics at another hospital for chronic bronchitis and emphysema. Heart size at that time had been normal. Four months later a systolic murmur was heard and mild cardiomegaly was noted; he was treated with antibiotics and bronchodilators again. Because of increasing heart size and cervical venous engorgement, a diagnosis of pericarditis was considered and the patient was transferred to a second hospital, where a diagnosis of pericardial effusion was made after cardiac catheterization. Left ventricular angiography showed poor contraction of this

Fig 1. Chest roentgenograms of Patient 1 (A) before operation, showing mild to moderate cardiomegaly, and (B) four months after aortic valve replacement, showing normal heart size.



chamber. Pericardicentesis yielded 350 ml of serosanguineous fluid. Most blood cultures were negative, but there was one report of a culture yielding coagulase-positive *S. aureus*.

He was transferred to our service, where he was found to be in Class IV congestive heart failure. His chest roentgenogram showed a cardiothoracic ratio of 60% (Fig 2A). An aortic diastolic and an Austin Flint murmur were heard, but peripheral signs of aortic regurgitation were absent. Cardiac catheterization yielded the findings shown in Table 2. The patient underwent aortic valve replacement.

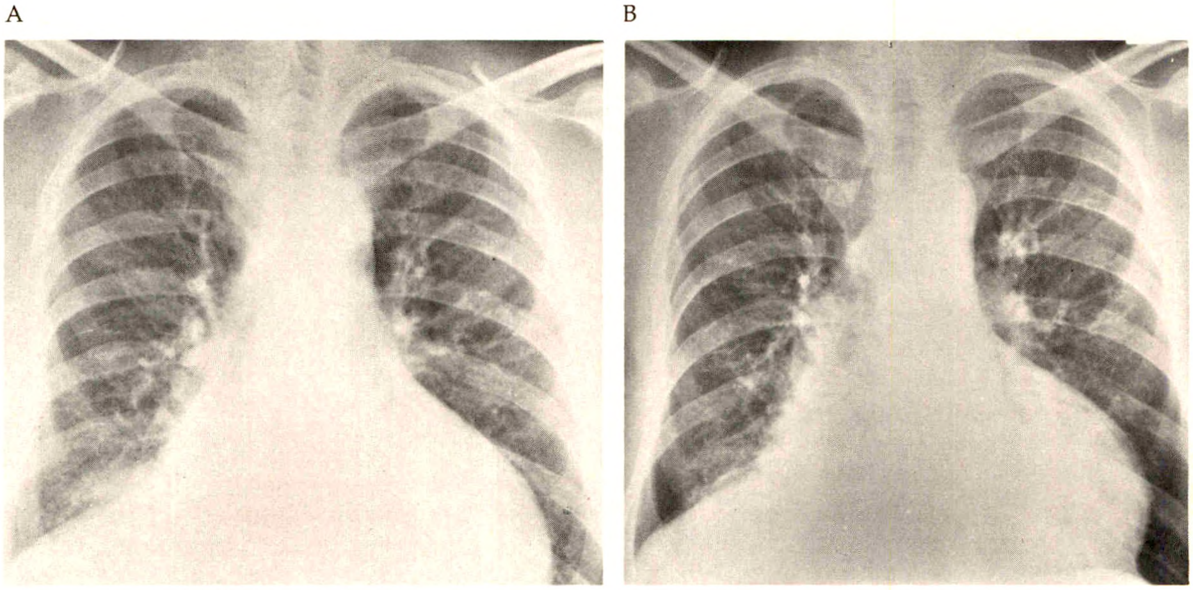
At operation the aortic valve was found to be bicuspid with fusion of the right and left leaflets. There was evidence of endocarditis in the posterior commissure, ie, between the noncoronary leaflet and the fused right and left leaflets, with prolapse of the left leaflet and detachment of the fused leaflet from its commissural support. Vegetation extended through the aortic wall and down into the myocardium surrounding the left atrium to the attachment of the anterior mitral leaflet.

The patient recovered from operation uneventfully. He has now been followed for two years and continues to be in congestive heart failure. His chest roentgenogram (Fig 2B) shows persistent cardiomegaly. A recent study showed an LVEDP of 33 mm Hg, pulmonary artery mean pressure of 35 mm Hg, and cardiac index of 2.2 L/min/m^2. This patient's course suggests that to delay operation for acute aortic regurgitation may result in significant residual left ventricular dysfunction.

Patient 4

T. P., a 52-year-old man with a known cardiac murmur of several years' duration, had an insidious onset of fatigue, petechial rash, arthralgia, chills, exertional dyspnea, and pedal edema. Six weeks before admission he had had a dental procedure performed without antibiotic coverage. Physical examination revealed congestive heart failure, murmurs of aortic insufficiency and possible mitral insufficiency, and an S_3 and S_4 gallop. The chest roentgenogram showed cardiomegaly with moderate lung congestion. His blood count revealed polymorphonuclear leukocytosis. Blood culture yielded *Streptococcus viridans*. In view of a history of penicillin allergy, the patient was treated with vancomycin and streptomycin. Penicillin desensitization was undertaken, and digitalis and diuretic therapy were started. He appeared to be improving clinically.

Fig 2. Chest roentgenograms of Patient 3 (A) a few weeks before operation, showing a markedly enlarged heart, and (B) two years after valve replacement, showing lack of improvement in heart size. The patient continued to be in Functional Class II to III.



On the sixth day of hospitalization the patient developed severe bradycardia due to complete heart block and died. Postmortem examination revealed rheumatic valvulitis involving the aortic and mitral valves and endocarditis of the aortic valve with perforation of the right and noncoronary cusps extending into and eroding the membranous interventricular septum with abscess formation. Penetration of the septum was stopped short by the medial leaflet of the tricuspid valve tethered to the septum. This was the only preoperative death in this series, and the history emphasizes that arrhythmia is an uncommon but serious threat to these patients.

Patient 5

W. R., a 65-year-old black man, was admitted to the emergency room in a severely obtunded, semicomatose condition. He was febrile (40°C), and there was evidence of nuchal rigidity and left hemiparesis. The peripheral blood yielded a leukocyte count of 24,000 with 90% polymorphonuclear leukocytes. The cerebrospinal fluid was xanthochromic with a pleocytosis of predominantly polymorphonuclear cells, a protein content of 190 mg/100 ml, and no detectable glucose. A grade 2/6 systolic ejection murmur was heard.

The patient was treated with antibiotics with the diagnosis of possible bacterial meningitis. Blood and cerebrospinal fluid cultures yielded group G beta-hemolytic streptococcus. Since subsequent cultures yielded *S. aureus*, he was treated with oxacillin for one week prior to operation. A cerebral angiogram did not reveal any evidence of abscess or subdural fluid collection. During treatment the patient developed an easily audible murmur of aortic insufficiency. Soon congestive heart failure supervened which initially appeared to respond to digitalis and diuretics. However, there were increasing signs of gross aortic insufficiency and he developed intractable pulmonary edema.

Operation was performed on an emergency basis after a total of five weeks of antibiotic therapy. Cardiac catheterization was not done. At operation the aortic valve was found to be tricuspid. The left leaflet was fragmented in several places and had vegetation on it. The right leaflet had a large hole in it near the commissure between the right and left leaflets, and the remainder of the valve was thickened. The noncoronary leaflet was normal. The aortic valve was excised and replaced by a No. 25 Björk-Shiley valve. He recovered uneventfully and is now asymptomatic. This patient was the only one in the series operated upon on an emergency basis.

Results

In 12 of 14 patients aortic valve replacement was undertaken electively because of continued congestive heart failure. In 1 patient (W. R.), operation was performed on an emergency basis because of intractable pulmonary edema. In another (A. D., see Table 1), valve replacement was undertaken because of multiple embolic episodes associated with congestive heart failure. In other patients with single embolic episodes, elective operation was performed after a course of adequate antibiotic therapy and stabilization of congestive heart failure. A bicuspid aortic valve was present in 3 patients. One or more valve leaflets were perforated or destroyed in all patients. Culture of the aortic valve was negative in all patients except for 1 with *Candida* endocarditis (J. W., Table 1). This patient was operated upon for the eradication of infection, even though congestive heart failure was clinically not significant.

Mortality

One patient in this series died during medical management from complete heart block of acute onset. At postmortem examination there was no evidence of coronary embolism, but the ventricular septum in the region of the bundle of His was eroded by an abscess. One patient died four weeks after replacement of the aortic valve, and postmortem examination revealed acute myocardial infarction, probably due to coronary embolism. Another patient died seven weeks after operation with a clinical picture of cerebrovascular accident. The surgical mortality was 14%; the overall mortality was 20%.

Follow-up

Mean duration of follow-up has been 18 months (range, 1 to 48 months). Of 11 patients who had been followed to October, 1974, 10 were in

NYHA Functional Class I (see Table 1). Only Patient 3 (R. C.) remained in Functional Class III due to left ventricular dysfunction. Three other patients continued to demonstrate mild cardiac enlargement on chest roentgenograms. The heart size was normal in the remainder of the patients. Four patients had an audible, soft aortic diastolic murmur without peripheral evidence of significant regurgitation.

Comment

In the absence of operative intervention, the development of aortic regurgitation due to infective endocarditis is associated with a mortality of approximately 50% [3] because of progressive hemodynamic deterioration. While intractable pulmonary edema or shock is a clear indication for prompt valve replacement, the proper timing of an operation in the face of lesser degrees of decompensation during active infection remains unclear.

Manhas and co-workers [13], in an analysis of 139 patients from the literature (including 24 of their own patients), found an early mortality of 27% for valve replacement during the active stage of infection versus 12% in the healed stage. In patients receiving more or less than three weeks of antibiotic therapy, the early surgical mortality was 19 and 32%, respectively. In 29 patients reported by Okies and associates [14] who underwent valve replacement during infective endocarditis, the hospital mortality in groups receiving incomplete and complete courses of antibiotic therapy was 7 of 15 (47%) and 1 of 14 (7%), respectively. While these data suggest that bloodstream and presumably valve sterilization is a desirable goal prior to operative intervention, this consideration must be balanced against continuing hemodynamic deterioration leading to irreversible myocardial damage. In a recent review of operations for infective endocarditis, Black and co-workers [1] found that the largest single cause of postoperative mortality was cardiovascular insufficiency. The incidence of this complication was 32%, of which the largest subset, or 67%, consisted of patients in whom cardiopulmonary bypass could not be discontinued. Both Manhas and colleagues [13] and Black and associates [1] attribute these findings to irreversible myocardial damage caused by the valve lesions.

Our experience with isolated aortic regurgitation due to infective endocarditis superimposed upon a previously functionally normal valve suggests that, generally, these patients eventually will require valve replacement. All patients in this series manifested clinical signs of significant congestive heart failure, and nearly all were in NYHA Functional Class III or IV prior to the institution of bed rest, salt restriction, and digitalis and diuretics therapy. Use of this medical regimen stabilized congestive heart failure adequately to keep these patients symptom free at rest and usually permitted a full course of antibiotic therapy prior to valve replacement. Only 1 patient required emergency valve replacement for intractable pulmonary edema. In the majority of patients the serious hemodynamic burden borne by the left ventricle was documented by cardiac catheterization (see Table 2). Gross elevation of LVEDP, pulmonary hypertension, depressed cardiac output, and 3 to 4+ aortic regurgitation were the characteristic findings. While hemodynamic studies in acute aortic regurgitation due to infective endocarditis are few, our findings are similar to those reported in severely symptomatic patients [1, 23, 25]. Nevertheless, we encountered no instances of inability to remove patients from cardiopulmonary bypass. The two postoperative deaths in our series were apparently the result of embolic episodes unrelated to myocardial failure.

The therapeutic implications of our results are limited to a particular subset of patients with endocarditic aortic regurgitation, ie, those in whom a medical regimen halts the progression of hemodynamic failure, though at a clinically overt level. If this condition is fulfilled, then the time spent in antibiotic administration does not lead to irreversible myocardial damage sufficient to influence the clinical results of operation. Significant delay beyond this period may terminate in irreversible myocardial disease, as evidenced by the history of Patient 3 (R. C.), in whom delay was the result of failure to arrive at the correct diagnosis. This patient continued to manifest cardiomegaly with catheterization evidence of left ventricular dysfunction in the absence of valve disease. The 5 other patients in this series who demonstrated preoperative cardiomegaly have improved to Functional Class I status with reduction in their heart size to normal limits. In these 5 patients the mean duration from the onset of symptoms to the time of operation was four months.

Our study did not determine the optimum timing for operation. The purpose of stabilizing congestive heart failure was to allow sterilization of the bloodstream prior to operative intervention. The advantage of this sterilization is a presumed reduction in the incidence of valve dehiscence and in new nidi of infection. Clinically, this should be reflected in a less frequent occurrence of persistent sepsis or significant periprosthetic regurgitation. While these complications were not encountered in our series, in which the mean duration of antibiotic therapy was five weeks, it is possible that similar results can be obtained after as little as two weeks of antibiotic therapy [4, 5, 24]. In three recent series [4, 13, 24] comprising a relatively extensive experience with valve replacement in infective endocarditis, the duration of antibiotic treatment was generally less than four weeks; persistent sepsis was a problem in only 3 of the 66 combined patients, and significant periprosthetic regurgitation requiring reoperation occurred in 3 (5%). Although these complications have a low incidence, the possibility that they may occur warrants consideration in determining the optimum timing for operation. Further, other factors may contribute to the higher early mortalities associated with incomplete antibiotic therapy. One of these is toxic myocarditis [16, 17, 20], though confirmation of its presence may be impossible in the face of hemodynamic alterations induced by free aortic regurgitation. On the basis of our experience, we therefore recommend a full course of antibiotic therapy in patients with acute aortic regurgitation if their heart failure can be stabilized on a medical regimen. This goal can be accomplished in a significant number of patients; in our hands, it has resulted in a relatively low postoperative mortality of 14% (Table 3).

Table 3. Early Mortality after Valve Replacement in Infective Endocarditis

Authors	No. of Patients	Early Mortality (%)
Hancock et al [7]	10	30
Okies et al [14]	32	31
Wise et al [25]	10	40
Crosby et al [4]	19	10
Windsor et al [24]	15	33
Manhas et al [13]	24	29
Present study	15	14

Embolism in our series constituted a relatively weak indication for urgent valve replacement. Multiple embolism unassociated with heart failure did not occur. Griffin and associates [6] have recommended prompt valve replacement even in patients with mild congestive heart failure in order to prevent sudden death due to coronary embolism. In our series coronary embolism occurred only once, and this was in the postoperative period. One sudden death did occur during medical therapy, but it was due to ventricular septal erosion producing complete heart block in the absence of coronary embolism. Fowler and associates [5] reported a similar experience with regard to sudden death, ie, this complication is more likely to be related to infection rather than to a major coronary embolus. The postmortem series reported by Robinson and Ruedy [19] also suggests that sudden death due to coronary embolism may occur after aortic valve replacement in infective endocarditis.

It is difficult to formulate a definitive policy regarding the role of embolism in determining the timing of operation since data are lacking concerning the risk of subsequent embolism following the first episode and embolism is a recognized complication of valve replacement [1, 13, 19]. In patient A. D. (Table 1), aortic valve replacement was performed after an incomplete course of antibiotic therapy because of recurrent embolism. This patient also manifested significant congestive heart failure. Since it was evident that valve replacement would be required, earlier operation was undertaken. In contrast, patient L. W. (Tables 1, 2) developed a septic embolus to the right femoral artery resulting in a mycotic aneurysm; his heart failure was moderately well controlled with medical therapy, and the mycotic aneurysm was resected without further embolic episodes. Valve replacement was delayed pending completion of the antibiotic course in 2 other patients following an embolic episode; there were no recurrences. In the absence of firm data, we consider systemic embolism a relatively weak indication for early valve replacement. An exception is fungal endocarditis; operation appears to be indicated at the time of diagnosis to eradicate infection [11, 22].

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Acute Penetrating Tracheal Trauma

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ABSTRACT **During the past ten years, 20 patients with acute penetrating tracheal injury (15 cervical and 5 thoracic) have been treated at Grady Memorial Hospital. Ten of the 20 patients had other major associated injuries: 6 had esophageal wounds, 5 had arterial injuries, and 2 had additional wounds.**

In the first 5 patients treatment of the tracheal injuries consisted of tracheostomy alone. Later on, the tracheal wounds were managed according to type, site, size, and the type of other organ injury. Repair of the tracheal wound and tracheostomy were done in 3 patients, repair of the tracheal wound and temporary tracheal intubation in 4 patients, tracheocutaneous stoma in 1 patient, temporary tracheal intubation alone in 4 patients, and observation alone in 3 patients.

Seventeen patients recovered from their injuries and 3 died from sepsis, respiratory insufficiency, or cerebrovascular accident. All 3 deceased patients had other major injuries.

This experience suggests that the treatment of penetrating tracheal injury should depend upon the type, size, and site of the wound and the type of coexistent injury to other organs, and that primary repair of the tracheal wound can be carried out in the majority of the patients.

With improved transportation of victims from the site of injury to medical facilities, more patients with severe penetrating injuries, including injuries to the tracheobronchial tree, survive the initial insult [1–6]. The purpose of this communication is to review our last ten years' experience with penetrating injuries to the trachea, with special emphasis on their management.

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Material and Methods

From 1966 to 1975, 20 patients with penetrating wounds of the trachea were treated at Grady Memorial Hospital (Table). Seventeen of them were male and 3 were female with ages ranging from 15 to 49 years, the average being 27 years. Fifteen of the patients had sustained injury to the cervical trachea, 12 from a bullet and 3 from a knife wound, and 5 had injuries to the thoracic trachea, all of them from a bullet wound.

Ten of the 20 patients had other major injuries in addition. Six had perforation of the esophagus, 5 had major arterial injuries, and 2 had other serious wounds. The esophagus was injured in the cervical region in 5 patients and in the thoracic region in 1 patient. The innominate artery was injured in 1 patient, the common carotid in 2, the subclavian in 1, and both the vertebral and the internal mammary arteries in 1. The other major injuries were a bullet wound of the urinary bladder in 1 patient and 8 bullet wounds of the small bowel, a bullet wound of the duodenum, and one of the spinal cord, region T1–T2, in another patient.

Upon admission to the hospital, 11 patients were in some respiratory distress and 6 had hemoptysis. In 2 of them, 1 of whom had complete transection of the cervical trachea, the hemoptysis was so severe that immediate tracheal intubation was performed to protect them from massive aspiration of blood. Subcutaneous emphysema in the supraclavicular and cervical region was observed in 17 patients; in 3 of them air was escaping from the cutaneous wound.

Roentgenograms of the chest or the cervical region, which were obtained in all patients, showed subcutaneous air in the neck in 10, pneumomediastinum in 4, pneumothorax in 4, and hemothorax in 3 patients. Due to the close proximity of the wound to the esophagus or because the missile had traversed the mediastinum, an esophagogram was obtained in 17 of

Site, Extent, Management, and Results of Penetrating Tracheal Wounds in 20 Patients

Patient's Age (yr) & Sex	Site of Tracheal Injury	Extent of Injury	Means of Diagnosis	Management of Tracheal Wounds	Result
22, F	Cervical	Single	Exploratory operation	Tracheostomy	Good
32, M	Cervical	Through-and-through	Tracheoscopy	Tracheostomy	Good
17, M	Thoracic	Single	Tracheoscopy	Tracheostomy	Good
35, M	Cervical	Through-and-through	Exploratory operation	Tracheostomy	Died
45, M	Cervical	Through-and-through	Bullet expectoration	Tracheostomy	Died
23, M	Cervical	Through-and-through	Tracheoscopy	Suture & tracheostomy	Hoarseness
24, M	Cervical	Through-and-through	Exploratory operation	Suture & tracheostomy	Good
21, M	Thoracic	Single	Exploratory operation	Suture & intubation	Good
49, M	Cervical	Through-and-through	Exploratory operation	Suture & tracheostomy	Good
31, M	Cervical	Single	Exploratory operation	Suture & intubation	Good
32, F	Thoracic	Single	Tracheoscopy	Suture & intubation	Died
22, M	Cervical	Single	Exploratory operation	Suture & intubation	Good
17, M	Cervical	Transection	Exploratory operation	Tracheocutaneous stoma	Tracheostomy
28, M	Cervical	Through-and-through	Tracheoscopy	Intubation	Good
31, M	Thoracic	Single	Tracheoscopy	Intubation	Good
30, M	Thoracic	Single	Tracheoscopy	Observation	Good
28, M	Cervical	Through-and-through	Tracheoscopy	Intubation	Good
15, F	Cervical	Single	Tracheoscopy	Observation	Good
25, M	Cervical	Not visualized	Not confirmed	Intubation	Good
29, M	Cervical	Not visualized	Not confirmed	Observation	Good

the 20 patients. Esophageal perforation was demonstrated in 4 of them.

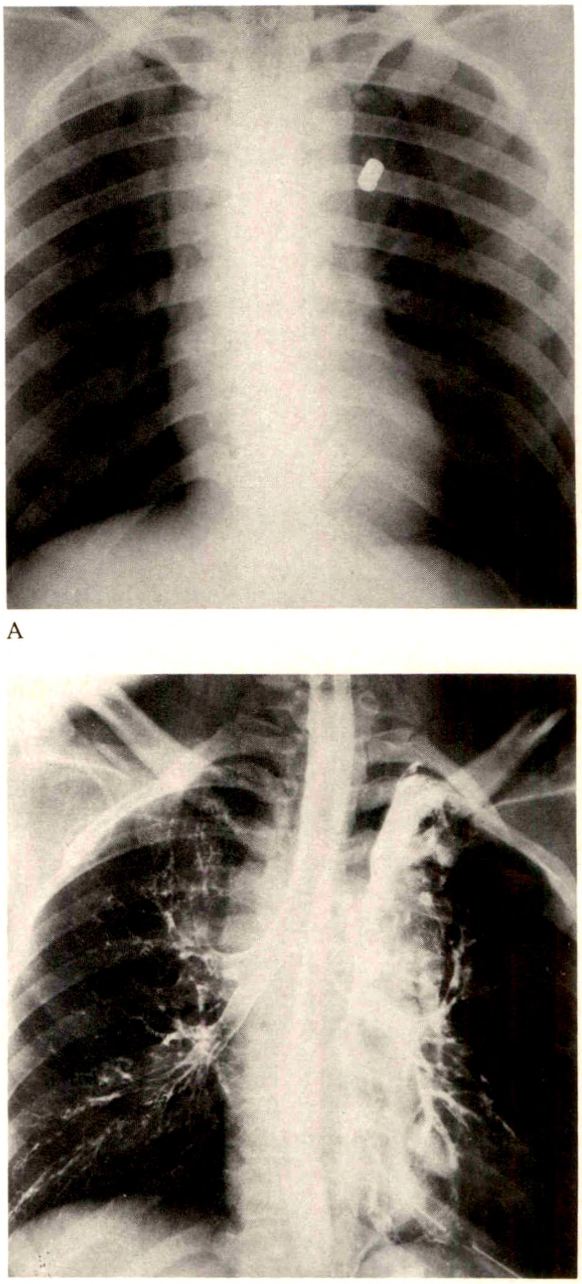
The diagnosis of tracheal injury was suspected from the location of the external wound, the history, the physical examination, and the roentgenographic findings. The diagnosis was confirmed by tracheoscopy in 9 patients, at the time of exploratory operation in 8 patients, and when a bullet was expectorated in 1 patient; in 2 patients the diagnosis was not confirmed. Exploratory operations were performed because a vascular or an esophageal injury was suspected. In 8 of the patients the tracheal wound was a "through-and-through" type, in 9 it involved only one side of the trachea, in 1 the cervical trachea was completely transected, and in 2 patients the tracheal injury was not visualized (see the Table).

The treatment of tracheal injury during the early part of our experience consisted of tracheostomy alone, performed in 5 of our patients. In the later period the tracheal wounds were managed according to their clinical presentation, the extent of injury, and other coexisting organ injuries. Repair of the tracheal wound and tracheostomy were done in 3 patients, repair of the tracheal wound and temporary orotracheal or nasotracheal intubation in 4 patients, tracheocutaneous stoma in 1 patient, temporary orotracheal or nasotracheal intubation in 4 patients, and observation alone in 3 patients (see the Table). The temporary tracheal intubation was maintained for 24 to 48 hours.

All cervical esophageal perforations and the innominate and common carotid artery wounds were primarily repaired, whereas the other injured vessels were ligated. The patient with thoracic esophageal perforation and injury of the trachea just above the carina (Figure), because of her very precarious condition and the gross contamination of the mediastinum, had primary repair of the tracheal wound, transection of the esophagus at the site of injury, exteriorization of its cephalad end as a cervical esophagostomy, suture of its distal end, and gastrostomy.

Seventeen patients recovered from their injuries and 3 died (see the Table). One patient with a gunshot wound of the cervical trachea and of the urinary bladder died on the fifth day after injury from aspiration pneumonia and a cerebrovascular accident. A patient with a bullet wound of the thoracic esophagus and trachea died on the sixth day following injury from pulmonary insufficiency and infection. The third patient, who had a bullet wound in the spinal cord (T1–T2) and paraplegia, a bullet wound of the cervical esophagus and duodenum, and multiple bullet wounds of the small bowel, died on the twenty-third day after injury from sepsis and respiratory insufficiency.

Fifteen of the 17 patients who recovered from their trauma have had no difficulty associated with the tracheal injury. One patient with a through-and-through penetrating cervical tracheal wound and esophageal perforation underwent repair of all wounds and tracheostomy. After the wounds had healed he had persistent hoarseness. Laryngoscopy showed right vocal cord paralysis, which was still unchanged at the fifth postoperative week when he was lost to follow-up. One patient has a permanent tracheostomy. He had suffered complete transection of the cervical trachea, which had retracted into the mediastinum, and perforation of the esophagus. The esophageal wound was primarily repaired, and after the end that had retracted into the mediastinum was retrieved, a tracheocutaneous stoma was created. On the fifth postoperative day he developed an esophagocutaneous fistula with some spilling of esophageal contents into the tracheostomy. After prolonged nasogastric feeding, the esophageal fistula closed and he was reoperated upon. At the time of the second operation the end of the proximal tracheal segment was revised, the tracheocutaneous stoma was removed, and end-to-end anastomosis of the trachea was performed. Postoperatively he developed severe subglottic stenosis necessitating an emergency tracheostomy, which he still has.



Admission radiological studies of a 32-year-old woman who had a bullet wound of the right second intercostal space. (A) Frontal chest roentgenogram shows the missile in the left lung field and widening of the mediastinal shadow. (B) Esophagogram showing a tracheoesophageal and pleuroesophageal fistula.

Comment

Penetrating wounds of the trachea are usually due to stab or bullet wounds, the latter being more common. The most frequent site of injury is the anterolateral wall of the cervical trachea, perhaps because that is its most unprotected part. The clinical manifestations of tracheal wounds depend upon the site and size of the wound and the type of injury to other organs. In general, hemoptysis and dyspnea of various degrees and subcutaneous emphysema of the neck are the most common symptoms and signs of penetrating tracheal injury. Small, isolated wounds of the cervical trachea usually become evident from subcutaneous emphysema in the neck, with or without blood-stained sputum. Larger, isolated wounds in this area may manifest themselves in the form of hemoptysis or massive subcutaneous emphysema if the cutaneous wound is sealed; if it is open, there may be air blowing through the cutaneous wound.

Isolated penetrating wounds of the thoracic segment of the trachea may appear with various degrees of hemoptysis and subcutaneous emphysema. Pneumothorax, with or without tension, or various degrees of respiratory and circulatory embarrassment may also be present. The latter findings depend upon the size of the wound, whether there is communication between the pleural space and tracheal lumen, and bidirectional or unidirectional flow of air from the lumen into the pleural space. Patients with unidirectional air flow from the trachea to the pleural space, because they frequently develop tension pneumothorax, are more likely to be severely symptomatic, whereas patients with an airway defect sealed with adjacent tissue are usually in no respiratory distress.

The diagnosis of a penetrating wound of the trachea should be suspected in all patients with a penetrating wound of the chest or neck, particularly when a bullet or knife has traversed the upper anterior mediastinum and when any of the previously mentioned clinical findings are present. The diagnosis should be confirmed with tracheoscopy if the patient's condition permits it.

The management of penetrating tracheal wounds should depend upon the type, size, and site of the wound and on the type of injury coexisting in other organs. Tracheal wounds shown by tracheoscopy to be small, with no loss of tracheal tissue, and with edges well apposed to each other can be treated effectively by temporary orotracheal or nasotracheal intubation. The cuff of the endotracheal tube should be inflated below the tracheal wound so that leakage of air through the wound into the mediastinal or subcutaneous tissue is prevented and the possible danger of contamination of these areas is avoided. The tracheal tube should be left in place for 48 hours, which is usually sufficient to allow the tracheal wound to seal. Large wounds of the trachea should be primarily repaired, as should the small ones that are explored on account of a suspected vascular or other organ injury. The repair should be done with interrupted 2-0 or 3-0 chromic catgut or other absorbable suture.

When both the trachea and the esophagus have been injured, they should be repaired primarily. In such a case, however, a flap of muscle if the injury is in the neck or in the inlet of the chest, or a flap of parietal pleura or pericardium if it is in the chest, should be appropriately constructed and interposed between the two suture lines so that the best possible healing of the wounds can be secured. In selected patients who have wounds of both the thoracic trachea and esophagus with gross contamination of the mediastinum, the trachea should be primarily repaired and a spit fistula, gastrostomy, and feeding jejunostomy should be performed. Two or three weeks later, after the tracheal wound heals, the esophagus can be appropriately reconstructed.

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Discussion

DR. JOHN R. BENFIELD (Los Angeles, CA): Dr. William Spenler and I recently summarized our experience with esophageal injuries from external sources (Arch Surg, 111:663, 1976). Because of the proximity of the esophagus to the trachea, our findings are relevant to today's nice presentation. As anticipated, our patients in whom the injuries were recognized promptly did well, and those in whom there was delayed recognition suffered a considerable incidence of complications. Two of 11 patients had false-negative esophagograms in the face of traumatic esophageal perforation. Thus, one lesson we learned is that patients suspected of having esophageal injury should undergo esophagoscopy and bronchoscopy as well as esophagography. Second, we included the first known report of esophageal disruption after a "whiplash" injury. Thus, I would urge that esophageal injury be kept keenly in mind and that the esophagus be fully evaluated to the limits of practicality whenever there is tracheal trauma of penetrating or blunt origin.

DR. AGUSTIN ARBULU (Detroit, MI): In a series of 22 tracheal lesions that we have observed at the Detroit General Hospital in the past five years, 6 were due to trauma, mainly stab wounds. It is extremely interesting to note that most of the injuries reported by Dr. Symbas were from gunshot wounds. In our area, gunshot wounds are usually close to the heart, so that the trachea is spared.

I think lesions of the trachea should be repaired later on—not as an emergency procedure. Ventilatory support can be provided through a tracheostomy, and the tracheal reconstruction can take place when other organ injuries have healed. In our experience, the majority of patients with gunshot wounds have multiple organ injuries and develop so-called shock lung, which requires repeated bronchoscopies in order to take care of respiratory problems. So I would like to utter a word of caution in relation to primary repair of tracheal injuries: our philosophy has been to reserve the permanent repair for a later date.

DR. SYMBAS: I thank Dr. Benfield and Dr. Arbulu for their fine comments. As to considering the possibility of a coexisting esophageal injury, we agree wholeheartedly that all patients with a penetrating tracheal wound should be investigated for this by esophagography, esophagoscopy, or at the time of exploratory operation.

In contrast to Dr. Benfield's experience, we have not had a false-negative esophagogram. The esophagogram is obtained in both frontal and lateral views, and chest roentgenograms are taken after the contrast material has passed into the stomach. This way, if a small amount of barium is extravasated from the esophageal lumen and is obscured by the barium in the esophagus, it would not be missed.

Dr. Arbulu, in Atlanta, too, victims are shot in the heart but also in the trachea. As was pointed out, we prefer to repair the tracheal wounds primarily whenever possible. This is done with chromic catgut, which, due to absorption of fluid after it is placed in the tissues, obliterates the needle holes and prevents air leak through them. Nor does it result in the formation of granulation tissue at the suture line, as is frequently the case when nonabsorbable suture is used, which necessitates later repeat bronchoscopies to extract suture material as well as granulation tissue.

Spectrum of Pulmonary Sequestration

M. Wayne Flye, M.D., Martin Conley, M.D., and Donald Silver, M.D.

ABSTRACT **Bronchopulmonary sequestration was diagnosed in 17 patients ranging in age from newborn to 64 years. The sequestration was intralobar in 14 patients and extralobar in 3. The spectrum of symptoms could be divided into three patterns: no symptoms (6 patients), respiratory problems (8 patients), and cardiovascular problems (3 patients). Cardiovascular problems usually manifest themselves in the first few weeks or months of life and often have a respiratory component. In older patients the sequestration is first manifested by recurrent pulmonary infections or, if it remains uninfected, an asymptomatic density on chest roentgenogram.**

The definitive diagnostic study is arteriography. Operative treatment for the intralobar variety consists of segmental resection or, if the inflammatory process is more extensive, lobectomy. An extralobar sequestration may simply be excised.

The term *pulmonary sequestration* is applied to a portion of lung that is separated completely (extralobar) or incompletely (intralobar) from normal functioning lung during early embryological development. It is supplied by an anomalous systemic artery that arises from the aorta or its branches between the base of the neck and the upper abdomen. The available evidence indicates that both types of sequestration develop as congenital foregut anomalies [8, 12, 15, 18, 21].

Typically the sequestration is discovered when the patient develops respiratory symptoms secondary to infections or associated cardiac anomalies. Some patients, however, remain asymptomatic, and the sequestration is suggested by a chest roentgenogram. This report of a series of pulmonary sequestrations demonstrates the spectrum of clinical manifestations that accompany the anomaly.

Clinical Material

Between 1960 and 1975, bronchopulmonary sequestration was diagnosed in 17 patients at the Duke University Medical Center (Table); during this period 11,120 patients were evaluated on the Cardio-Thoracic Service. The patients ranged in age from newborn to 64 years, and 10 of the 17 patients were male. The patients demonstrated one of three classic patterns: no symptoms, respiratory symptoms, or cardiovascular problems.

In 3 patients the sequestration was extralobar. In the 14 patients with the intralobar variety the sequestration was confined to the lower lobes—8 on the left and 6 on the right. The vascular supply to the sequestration was by way of a single large systemic artery arising from either the thoracic or the abdominal aorta in all but 4 patients. In 3 of these 4 patients multiple smaller arteries from the aorta supplied the sequestration, while in a newborn with extralobar sequestration, postmortem examination demonstrated a single artery arising from the superior mesenteric artery. Venous drainage of the sequestration was through the inferior pulmonary vein to the left atrium in all but 1 patient, who had a left lower lobe intralobar sequestration that drained through a single intercostal vein above the diaphragm. The vascular anatomy was demonstrated by angiography in 8 patients and by postmortem examination in 2. In 7 patients the diagnosis was made at the time of operation; the correct diagnosis had been suspected preoperatively in 1 of them. In 3 of the 7 an asymptomatic, rounded density had been identified on chest roentgenogram, 2 patients had infected cavities, 1 had bronchiectasis by bronchogram, and 1 had a rounded density and chest pain.

Respiratory symptoms alone were present in 8 patients, 6 of whom gave a history of recurrent pneumonia. In 1 of the 6 patients with pneumonia, bronchography demonstrated bronchiectasis in the area of the sequestration; another patient had hemoptysis. In a seventh patient the

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Pulmonary Sequestration in 17 Patients, 1960–1975

No. of Patients	Age	Symptoms	Location & Type	No. of Arteries	Treatment	Results
Cardiovascular Problems						
3	Birth–22 mo	Congestive heart failure, 2; bilateral pneumothorax, 1	RLL, 2I; R, 1E	Single, all 3	Ligation, 2; none, 1	Died, 3
Respiratory Problems						
8	10 mo–43 yr	Recurrent pneumonia, 6; chest pain, 1; respiratory distress, 1	RLL, 3I; LLL, 3I; R, 1E L, 1E	Single, 6; three, 2	Lobectomy, 6; pneumonectomy, 1; none, 1	Improved, 7; died, 1
Asymptomatic						
6	2–64 yr	None, 5; heart murmur, 1	RLL, 1I; LLL, 5I	Single, 4; two, 2	Lobectomy, 3; segmentectomy, 2; none, 1	Improved, 6

RLL = right lower lobe; R = right pleural cavity; LLL = left lower lobe; L = left pleural cavity; I = intralobar; E = extralobar.

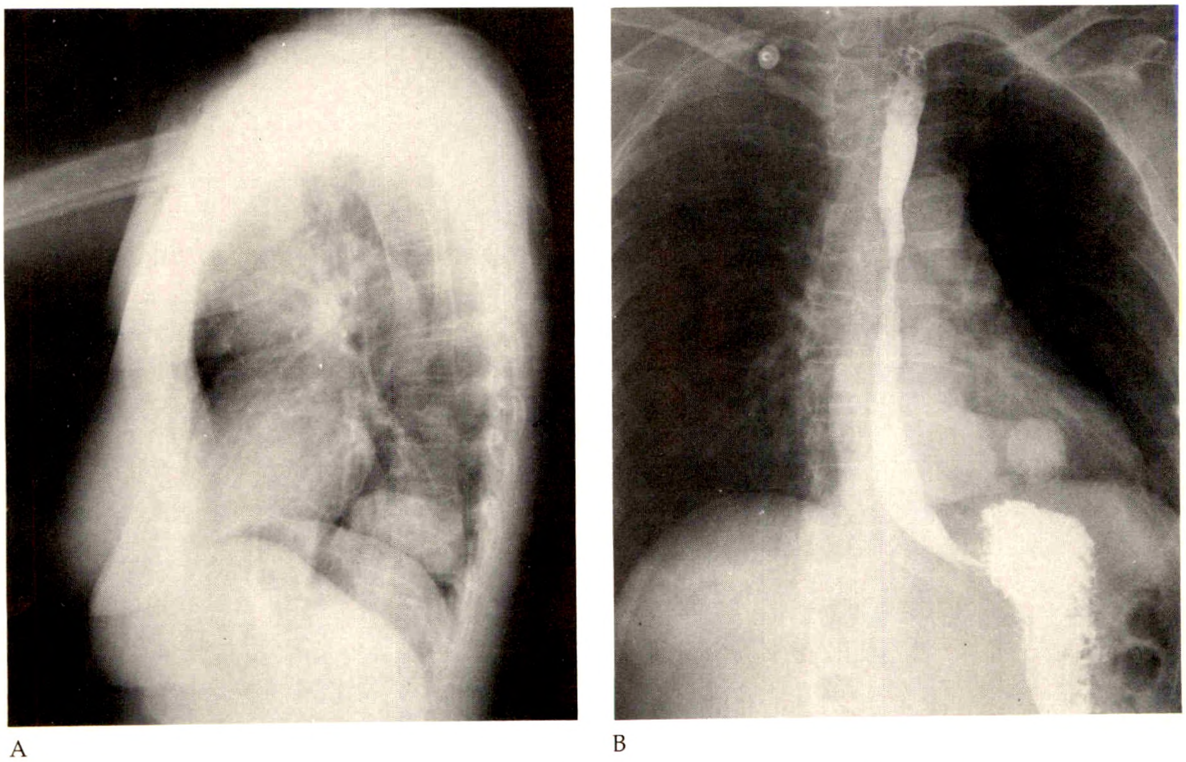
abnormality was discovered on chest roentgenogram while anterior chest pain was being evaluated, and in 1 newborn the diagnosis was made at postmortem examination.

The associated cardiovascular problems consisted of septal defects in 2 patients (1 ventricular, 1 atrial) and total anomalous pulmonary return with cor biloculare in a third. In the patients with septal defects, the extent to which shunting through the sequestration contributed to the development of congestive heart failure could not be determined. A 24-month-old child with an ostium primum defect did undergo ligation of the anomalous artery alone with symptomatic improvement of congestive heart failure. This patient, however, died at home two months later of uncertain cause. A second patient, with ventricular septal defect and peripheral pulmonic stenosis, died shortly after closure of the VSD and ligation of the anomalous artery. The third patient, who had cor biloculare, died of bilateral pneumothoraces several hours after birth, and the diagnosis was made at postmortem examination.

Six of the patients were asymptomatic and ranged in age from 2 to 64 years. In the 2-year-old the sequestration was discovered during cardiac catheterization for evaluation of a heart murmur. The remaining 5 patients were found to have asymptomatic masses by chest roentgenogram.

Nine of the 17 patients underwent lobectomy, 2 had segmental resection, 1 had a pneumonectomy, and the 2 patients with septal defects had simple ligation of the systemic artery without removal of the sequestration. In 2 newborns the diagnosis was made at postmortem examination. A 56-year-old woman with an asymptomatic sequestration demonstrated by arteriography refused operation and is currently being followed (Fig 1). All surviving patients have remained asymptomatic.

Postoperative complications occurred in 3 patients. A persistent pleural air leak necessitating chest tube suction for fourteen days developed in a 26-year-old woman. Mediastinal tamponade and death six hours following ligation of the anomalous artery and repair of a VSD occurred in a 14-week-old boy. A 32-year-old man developed massive postoperative bleeding following right lower lobectomy for an asymptomatic intralobar sequestration. A preoperative arteriogram had demonstrated that the arterial blood supply was derived from the intercostal and right inferior phrenic arteries (Fig 2). Multiple vessels were encountered in the area where the sequestration adhered to the chest wall. Despite care in ligating them, on reexploration one of these arteries was found to have retracted and was freely bleeding. Ten units of blood were required for transfusion. The patient's postoperative course was sub-



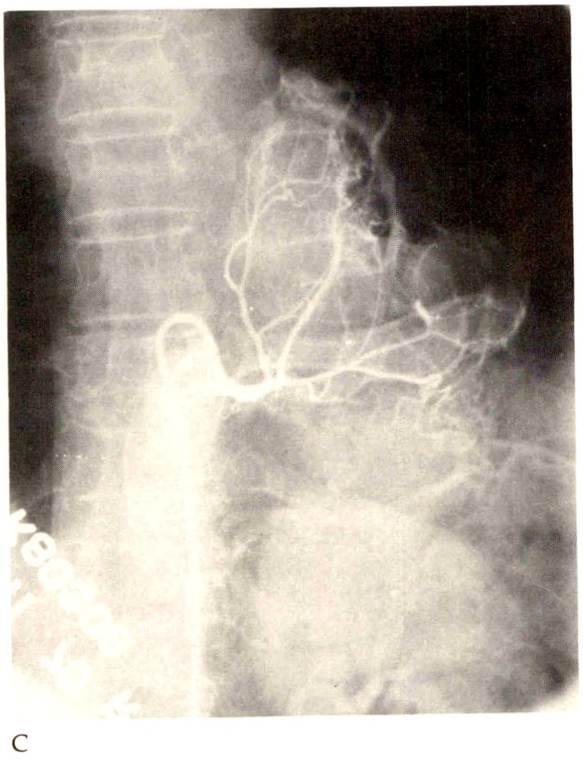


Fig 1. (A) Asymptomatic left lower lobe multilobular sequestration in a 56-year-old woman. (B) Barium swallow reveals no esophageal communication. (C) Selective arteriography demonstrates a single large systemic artery arising from the thoracic aorta and supplying the sequestration.

sequently uncomplicated, and he has remained asymptomatic.

Comment

Pulmonary sequestration can be viewed as disruption of morphogenesis in the region of the primitive foregut. Although most cases conform to the common features described for the intralobar and extralobar types of sequestration, many anatomical locations, types of vascular supply, and associated gastrointestinal and diaphragmatic anomalies have also been reported which are not well explained by any of the proposed theories [5, 10, 16]. Blesovasky [1] maintains that these are variants of the same process and that an embryonic organizer defect must be the fundamental lesion.

The spectrum of clinical symptoms is determined by the combination of anatomical anomalies. Although many lesions may remain asymptomatic, others will develop symptoms.

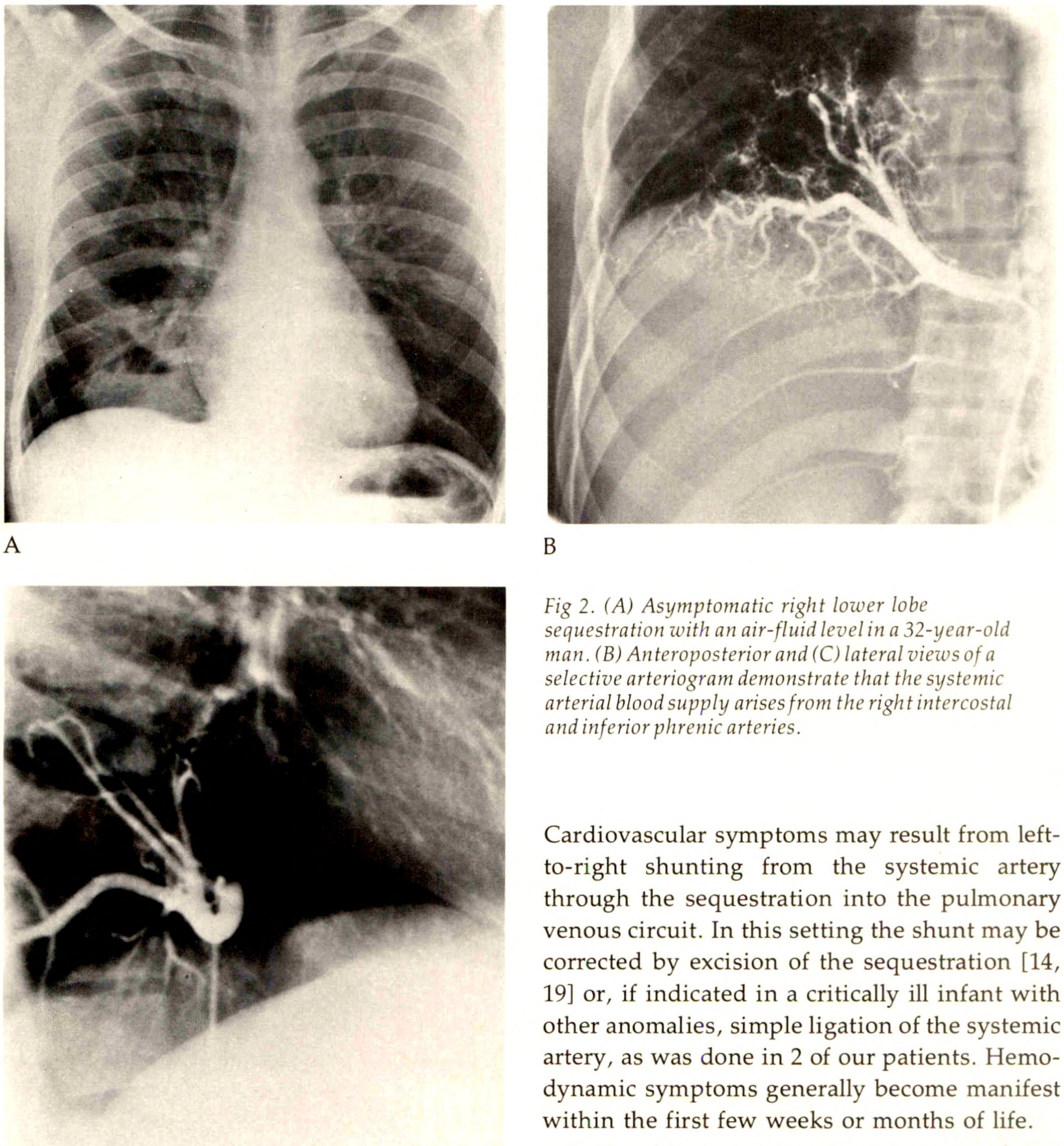


Fig 2. (A) Asymptomatic right lower lobe sequestration with an air-fluid level in a 32-year-old man. (B) Anteroposterior and (C) lateral views of a selective arteriogram demonstrate that the systemic arterial blood supply arises from the right intercostal and inferior phrenic arteries.

Cardiovascular symptoms may result from left-to-right shunting from the systemic artery through the sequestration into the pulmonary venous circuit. In this setting the shunt may be corrected by excision of the sequestration [14, 19] or, if indicated in a critically ill infant with other anomalies, simple ligation of the systemic artery, as was done in 2 of our patients. Hemodynamic symptoms generally become manifest within the first few weeks or months of life.

In the older age group, symptoms are almost invariably related to the presence of an airway communication. Recurrent fever, chills, and purulent sputum production are the most common signs. Bronchial communication is virtually unknown in extralobar sequestration [3], although symptoms have been reported secondary to progressive enlargement when a gastrointestinal communication persists [7]. Similarly, bronchial communication is initially absent in intralobar sequestration as well [13]; however, secretion of mucus within an intralobar sequestration causes a cystic swelling with subsequent compression and atelectasis of the surrounding normal lung tissue. Superimposed infection then spreads easily to the sequestration itself, causing capsular erosion and airway communication and thus producing the clinical picture typically associated with pulmonary sequestration.

Any indolent process seen on chest roentgenogram should alert one to the possibility of sequestration, especially if the posterior basilar region is involved [3]. If a pneumonic process is present, a multicystic lesion may be confused with pneumatoceles and operation consequently may be delayed. Bronchography may show displacement of adjacent segmental bronchi. The definitive diagnostic study, however, is the demonstration of a systemic arterial blood supply by arteriography [17].

Treatment of intralobar sequestration generally is operative resection, preferably after treatment of the acute inflammatory process. Lobectomy has been required in the majority of patients because of changes secondary to infection. Segmentectomy, however, has in 15 to 20% of cases been shown to be technically feasible without additional morbidity [20].

If an intralobar sequestration is nonaerated and the arteriogram is pathognomonic, nonoperative management may be considered under unusual circumstances [21]. In the case of diagnosed extralobar sequestration, observation rather than operation may be more strongly considered because of the very low incidence of associated problems.

The surgeon operating for any cystic or suppurative process within the thorax must be aware of the diagnosis of sequestration and the possibility of unusual vascular connections or unsuspected gastrointestinal communications. The occasional fatal consequence of inadvertent transection of an anomalous systemic artery has been well documented [2, 4, 6, 9, 11].

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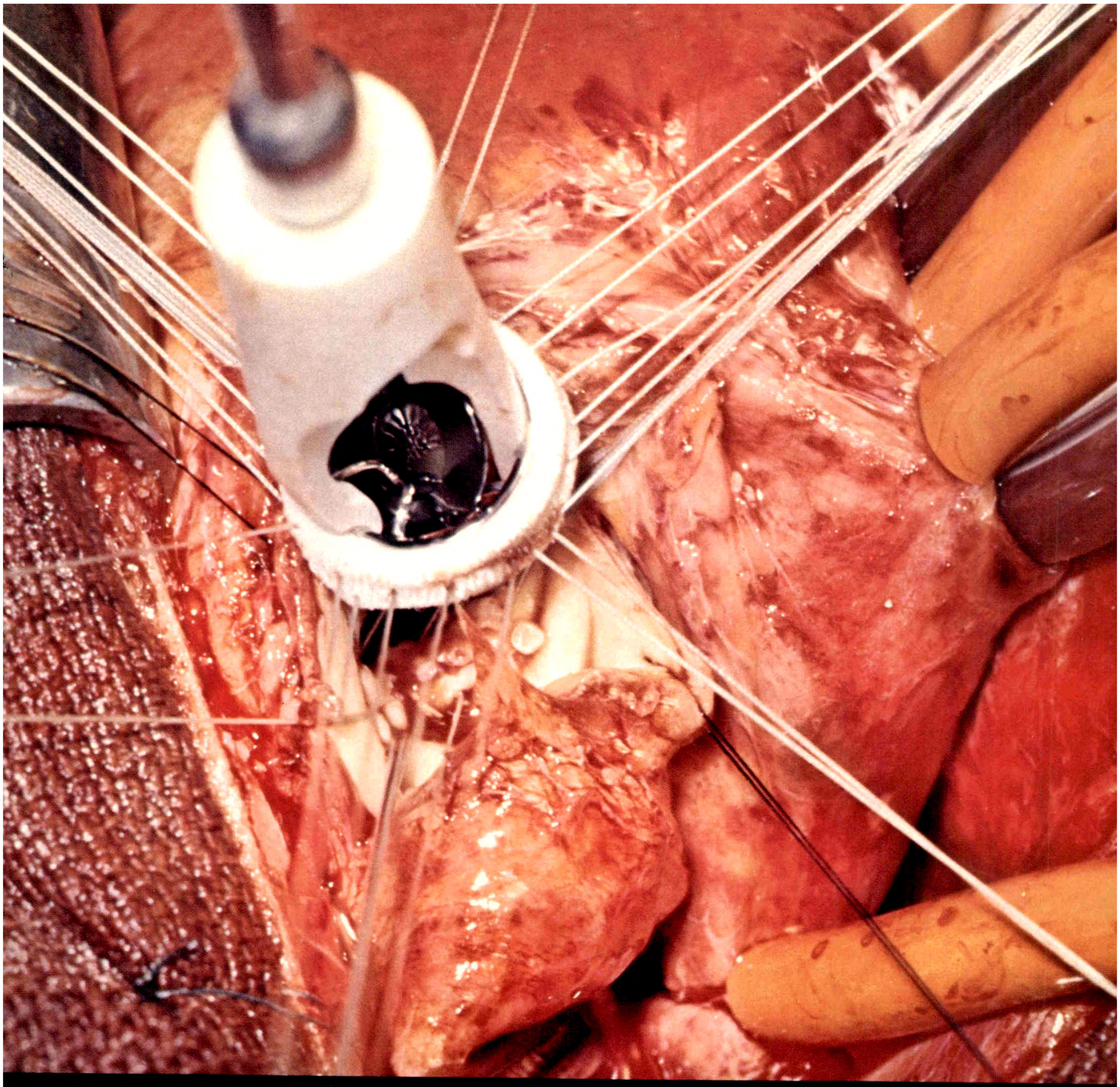

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*Bauer, A.W., Kirby, W.M.M., Sherris, J.C., and Turck, M.: Antibiotic Testing by a Standardized Single-Discs Method, Am. J. Clin. Pathol., 45:493, 1966; Standardized Disc Susceptibility Test, FEDERAL REGISTER 37:20527-29, 1972.

Indications: Although the principal indication for nafcillin sodium is in the treatment of infections due to penicillinase-producing staphylococci, it may be used to initiate therapy in such patients in whom a staphylococcal infection is suspected. (See Important Note below.)

Bacteriologic studies to determine the causative organisms and their sensitivity to nafcillin sodium should be performed.

In serious, life-threatening infections, oral preparations of the penicillinase-resistant penicillins should not be relied on for initial therapy.

Important Note: When it is judged necessary that treatment be initiated before definitive culture and sensitivity results are known, the choice of nafcillin sodium should take into consideration the fact that it has been shown to be effective only in the treatment of infections caused by pneumococci, Group A beta-hemolytic streptococci and penicillin G-resistant and penicillin G-sensitive staphylococci. If the bacteriology report later indicates the infection is due to an organism other than a penicillin G-resistant staphylococcus sensitive to nafcillin sodium, the physician is advised to continue therapy with a drug other than nafcillin sodium or any other penicillinase-resistant semi-synthetic penicillin.

Recent studies have reported that the percentage of staphylococcal isolates resistant to penicillin G outside the hospital is increasing, approximating the high percentage of resistant staphylococcal isolates found in the hospital. For this reason, it is recommended that a penicillinase-resistant penicillin be used as initial therapy for any suspected staphylococcal infection until culture and sensitivity results are known.

Methicillin is a compound that acts through a mechanism similar to that of nafcillin sodium against penicillin G-resistant staphylococci. Strains of staphylococci resistant to methicillin have existed in nature and it is known that the number of these strains reported has been increasing. Such strains of staphylococci have been capable of producing serious disease, in some instances resulting in fatality. Because of this there is concern that widespread use of the penicillinase-resistant penicillins may result in the appearance of an increasing number of staphylococcal strains which are resistant to these penicillins.

Methicillin-resistant strains are almost always resistant to all other penicillinase-resistant penicillins (cross resistance with cephalosporin derivatives also occurs frequently). Resistance to any penicillinase-resistant penicillin should be interpreted as evidence of clinical resistance to all, in spite of the fact that minor variations in **in vitro** sensitivity may be encountered when more than one penicillinase-resistant penicillin is tested against the same strain of staphylococcus.

Contraindications: A history of allergic reaction to any of the penicillins is a contraindication.

Warnings: Serious and occasionally fatal hypersensitivity (anaphylactoid) reactions have been reported in patients on penicillin therapy. Although anaphylaxis is more frequent following parenteral therapy it has occurred in patients on oral penicillins. These reactions are more apt to occur in individuals with a history of sensitivity to multiple allergens.

There have been reports of individuals with a history of penicillin hypersensitivity reactions who have experienced severe hypersensitivity reactions when treated with a cephalosporin. Before therapy with a penicillin, careful inquiry should be made concerning previous hypersensitivity reactions to penicillins, cephalosporins, and other allergens. If an allergic reaction occurs, appropriate therapy should be instituted, and discontinuation of nafcillin therapy considered. The usual agents (antihistamines, pressor amines, corticosteroids) should be readily available.

Precautions: As with any potent drug, periodic assessment of organ system function, including renal, hepatic and hematopoietic, should be made during prolonged therapy.

The possibility of bacterial and fungal overgrowth should be kept in mind during long-term therapy. If overgrowth of resistant organisms occurs, appropriate measures should be taken.

The oral route of administration should not be relied upon in patients with severe illness, or with nausea, vomiting, gastric dilatation, cardiospasm or intestinal hypermotility.

Safety for use in pregnancy has not been established.

Particular care should be taken with intravenous administration because of the possibility of thrombophlebitis.

Adverse Reactions: Reactions to nafcillin sodium have been infrequent and mild in nature. As with other penicillins, the possibility of an anaphylactic reaction or serum sickness-like reactions should be considered. A careful history should be taken. Patients with histories of hay fever, asthma, urticaria, or previous sensitivity to penicillin are more likely to react adversely.

The few reactions associated with the intramuscular use of nafcillin sodium have been skin rash, pruritus, and possible drug fever. As with other penicillins, reactions from oral use of the drug have included nausea, vomiting, diarrhea, urticaria, and pruritus.

Parenteral Administration: It is recommended that parenteral therapy be used initially in severe infections. The patient should be placed on oral therapy with this product as soon as the clinical condition warrants. Very severe infections may require very high doses.

Intravenous Route: The required amount of drug should be diluted in 15 to 30 ml. of Sterile Water for Injection, U.S.P., or Sodium Chloride Injection, U.S.P., and injected over a 5- to 10-minute period. This may be accomplished through the tubing of an intravenous infusion if desirable.

Stability studies on nafcillin sodium at concentrations of 2 mg/ml and 30 mg/ml in the following intravenous solutions indicate the drug will lose less than 10% activity at room temperature (70° F.) during the time period stipulated:

Isotonic sodium chloride	24 hours
5% dextrose in water	24 hours
5% dextrose in 0.4% sodium chloride solution	24 hours
Ringer's solution	24 hours
M/6 sodium lactate solution (conc. of 30 mg/ml)	24 hours

Discard any unused portions of intravenous solutions after 24 hours.

Only those solutions listed above should be used for the intravenous infusion of Unipen® (nafcillin sodium). The concentration of the antibiotic should fall within the range of 2 to 30 mg/ml. The drug concentrate and the rate and volume of the infusion should be adjusted so that the total dose of nafcillin is administered before the drug loses its stability in the solution in use.

There is no clinical experience available on the use of this agent in neonates or infants for this route of administration.

This route of administration should be used for relatively short-term therapy (24-48 hours) because of the occasional occurrence of thrombophlebitis, particularly in elderly patients.

Intramuscular Route: The clear solution should be administered by deep intragluteal injection immediately after reconstitution. After reconstitution, keep refrigerated (2°-8° C.) and use within 7 days or keep at room temperature (25° C.) and use within 3 days.

Oral Administration: Beta-hemolytic streptococcal infections should be treated for at least 10 days to prevent development of acute rheumatic fever or glomerulonephritis.

If oral therapy is inadequate, resort to parenteral nafcillin sodium.

After mixing, the oral solution must be stored in a refrigerator. Discard any unused portion after one week.

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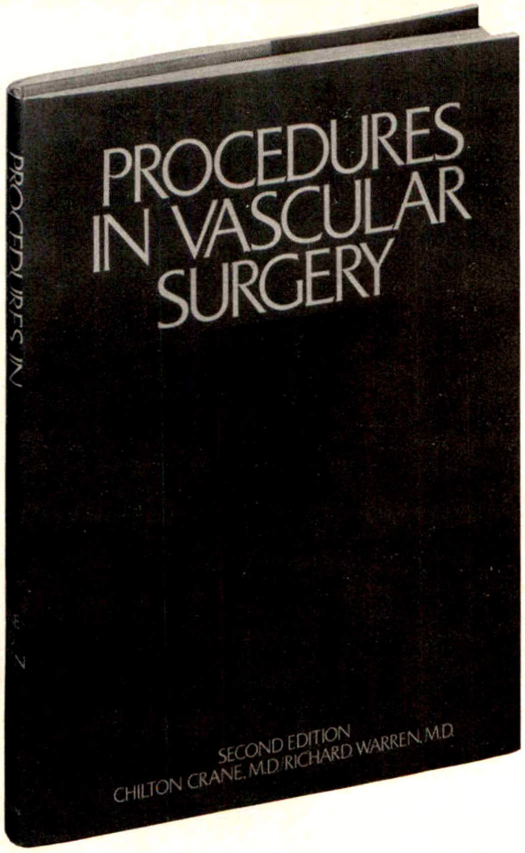
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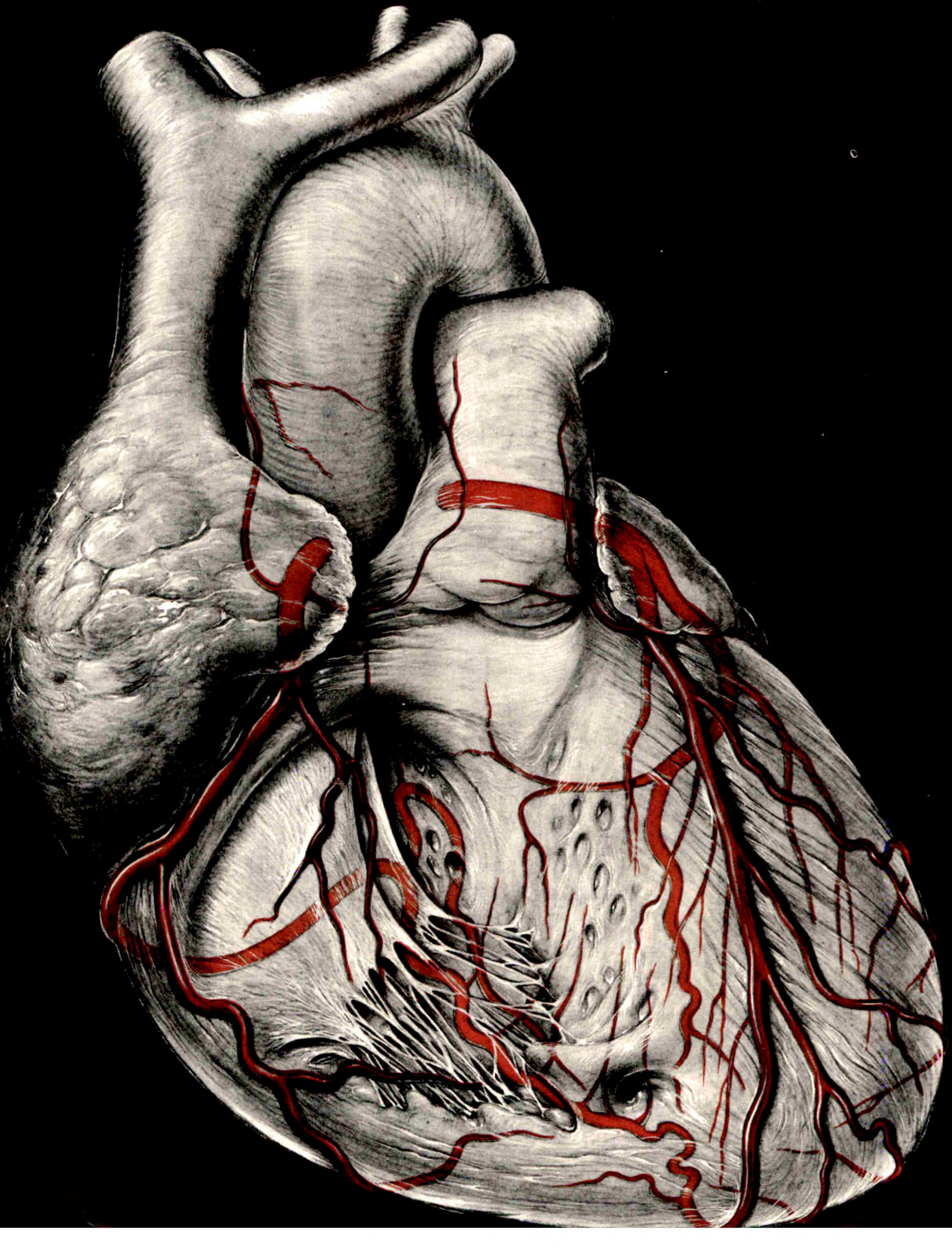

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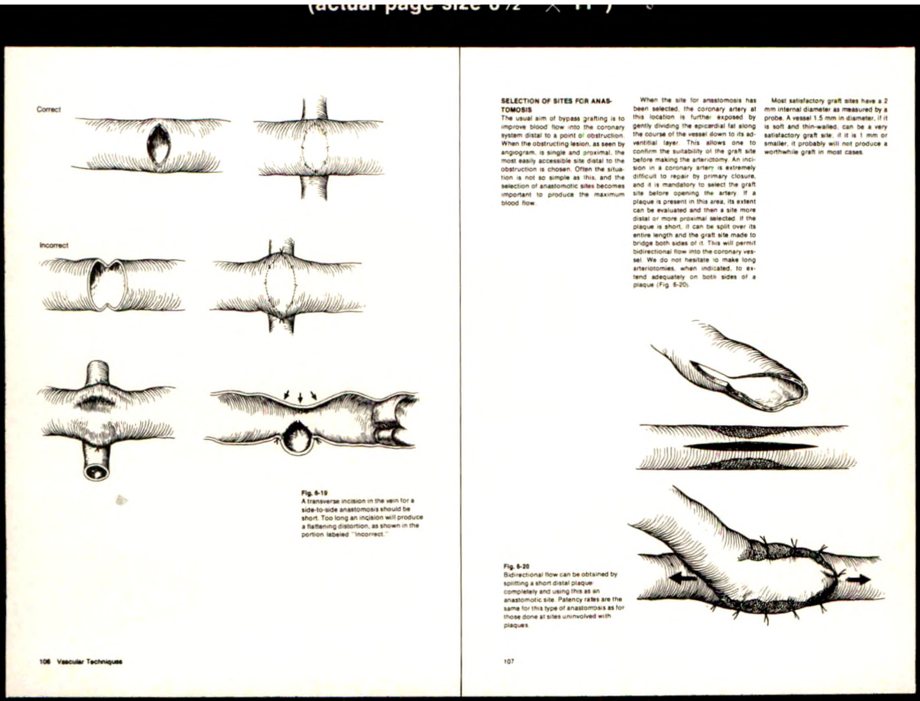
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Incorrect

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Most satisfactory graft sites have a 2 mm internal diameter as measured by a probe. A vessel 1.5 mm in diameter, if it is soft and thin-walled, can be a very satisfactory graft site; if it is 1 mm or smaller, it probably will not produce a worthwhile graft in most cases.

Fig. 6-19
A transverse incision in the vein for a side-to-side anastomosis should be short. Too long an incision will produce a flattening distortion, as shown in the portion labeled "Incorrect."

Fig. 6-20
Bidirectional flow can be obtained by splitting a short distal plaque completely and using this as an anastomotic site. Patency rates are the same for this type of anastomosis as for those done at sites uninvolved with plaques.

106 Vascular Techniques

107

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Intrathoracic Presentation of Amebic Liver Abscess

Mustafa I. Ragheb, M.S., Adel A. Ramadan, M.S.,
and Mohamed Ali H. Khalil, M.S.

ABSTRACT **Amebic infection is endemic in tropical and subtropical countries and still remains a common cause of chronic morbidity in these areas. This is a report of 10 patients with different intrathoracic presentations of amebic liver abscess who were treated surgically after conservative measures had failed. Five of these patients had empyema when first seen, 3 had lung abscess, and 1 had intrathoracic shadow that proved on exploration to be an amebic liver abscess. All these 9 patients had abscesses on the right side secondary to amebic liver abscess of the right lobe of the liver. The tenth patient had amebic pericarditis secondary to amebic abscess of the left lobe of the liver. Failure of conservative treatment in these patients is attributed to the thick nature of the amebic pus and the severe reaction of the pleura and pericardium to the amebic infection. To avoid the serious complication of pleuropulmonary amebiasis, early operation is advised for large liver abscesses that are unlikely to be controlled by conservative treatment. Transpleural drainage of such abscesses gives direct approach to their sites, which are commonly located in the superior part of the right lobe of the liver. Such drainage has proved to be safe provided that the patient is receiving antiamebic drug treatment.**

Amebic infection caused by the protozoan parasite *Entamoeba histolytica* is a widespread endemic infection in many of the tropical and subtropical areas of the world. Despite the common use of antiamebic drugs, it still remains one of the foremost causes of chronic morbidity in the endemic areas [1, 4, 11]. Amebic infection is either intestinal, producing amebic dysentery, or extraintestinal, producing mainly amebic hepatitis. *Entamoeba histolytica* gains access to the colon following ingestion of food or drink contaminated with the cysts of the parasite. In the stomach the wall of the cysts is digested, liberating the parasite, which through its cytolytic enzymes finds its way to the submucosa of the colon, where it produces the characteristic flask-shaped ulcers. At any time during this phase of amebic colitis, *E. histolytica* may erode branches of the portal vein and reach the liver as emboli in the portal blood.

Once established in the liver sinusoids, the amebae produce cytolytic destruction in the liver. This process may be diffuse, giving rise to diffuse amebic hepatitis, or localized, producing an amebic liver abscess, which is commonly found in the right lobe of the liver and less often in the left lobe. Characteristically, the abscess is solitary, containing chocolate brown or anchovy-colored saucelike pus that is sterile on culture. Amebic liver abscess may be secondarily infected; it may rupture in the sub-phrenic area or general peritoneal cavity; it may erode the diaphragmatic opening in the pleura, producing empyema; or it may work its way into the lung, giving rise to lung abscess. Pleuropulmonary complications are more common on the right side, but the left lobe abscess may open into the left side and, rarely, into the pericardium.

Clinical Material and Methods

From 1966 to 1975, 10 patients with different intrathoracic presentations of amebic liver abscess were treated surgically in our Cardio-Thoracic Surgery Unit after conservative management failed. Five of these patients had right-sided empyema, 3 others had right lung abscess, and another had what was diagnosed as a right intrathoracic shadow but proved on exploration to be an uncomplicated abscess in the right lobe of the liver. The tenth patient had amebic pericarditis secondary to left lobe abscess of the liver (Table). All these patients were men; their ages ranged from 17 to 40 years with a mean of 37.5 years. At one stage these patients were diagnosed clinically as having

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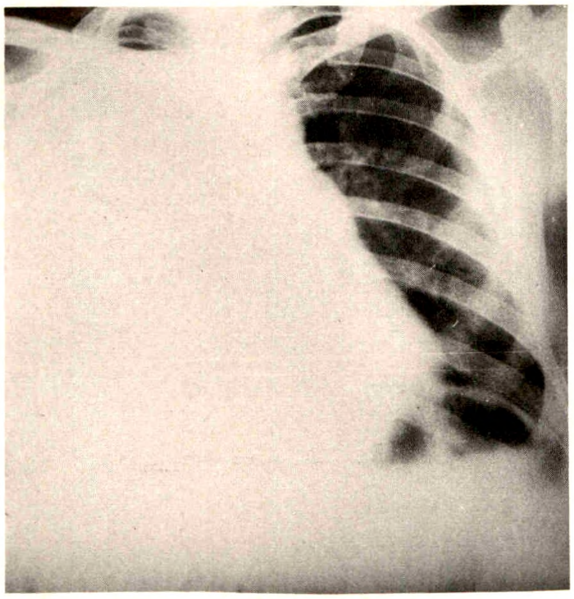
Types of Intrathoracic Amebiasis and Their Surgical Management

Intrathoracic Lesion	No. of Patients	Operation
Right empyema	4	Decortication & drainage of liver abscess
Right empyema with hepatobronchial fistula	1	Decortication & transpleural drainage of liver abscess
Right lung abscess		
Middle lobe	1	Middle lobectomy & intrathoracic drainage of liver abscess
Lower lobe	1	Lower lobectomy & transpleural drainage of liver abscess
Middle and lower lobe	1	Middle & lower lobectomy, then transpleural drainage of liver abscess
Intrathoracic shadow "liver abscess"	1	Transpleural drainage
Amebic pericarditis	1	Pericardiectomy

Fig 1. Right amebic empyema. This patient had hepatobronchial fistula through the middle lobe.



amebic liver abscess and they received full courses of antiamebic treatment in the form of emetine hydrochloride, chloroquine, and tetracyclines. The intrathoracic complications occurred either during or sometime after the course of drug treatment.

Pleuropulmonary Amebiasis

All 8 patients with pleuropulmonary amebiasis had it on their right side. Of the 8, 5 had pleural amebiasis in the form of empyema, 1 with hepatobronchial fistula manifested by the coughing up of characteristic amebic pus (Fig 1). The 3 other patients had pulmonary amebiasis in the form of a lung abscess (Fig 2).

The main presenting symptoms that indicated the pleuropulmonary complications were dyspnea together with a dull, aching pain of pleuritic nature that was referred to the right shoulder in 3 patients. Coughing up of amebic pus is a pathognomonic sign of hepatobronchial fistula; this was found in 1 patient with empyema. Mild hemoptysis was found in 2 patients with lung abscess. Mild to moderate temperature elevation ranging from 37.5° to 38°C was a common finding among these patients. The right lobe of the liver was enlarged both upward and downward, and intercostal tenderness could be elicited in all the patients with pleuropulmonary

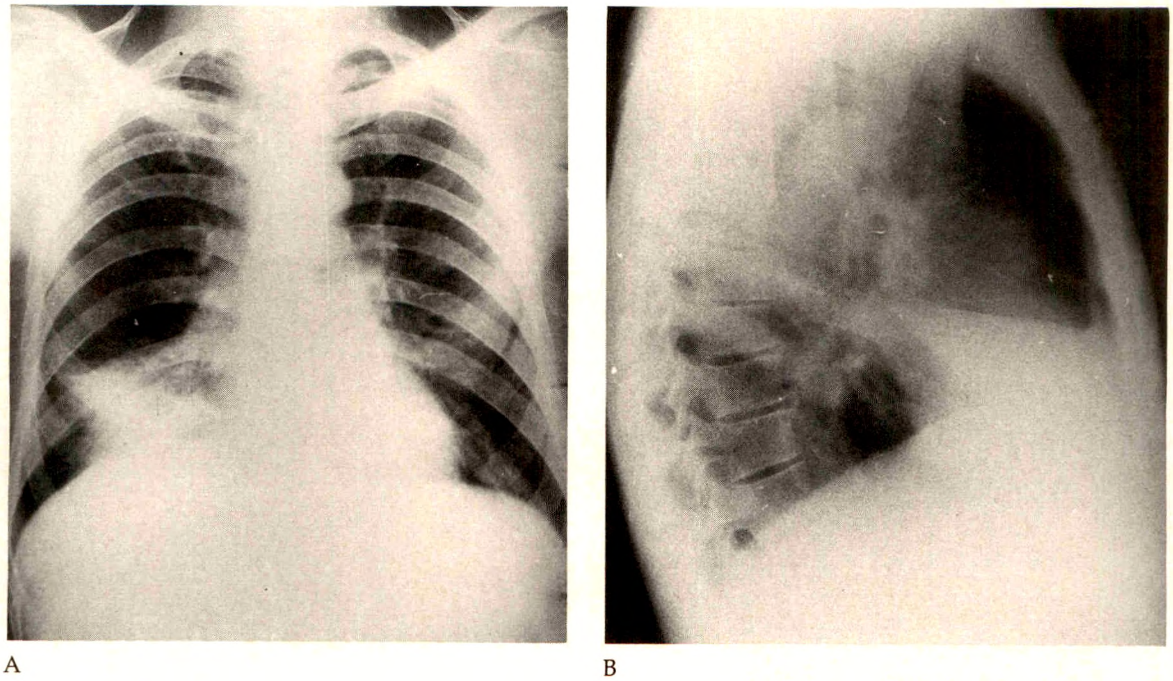


Fig 2. (A) Middle lobe amebic abscess. (B) Right lateral view of the same patient.

amebiasis, mainly in the midaxillary line of the eighth and ninth intercostal spaces. None of the patients were jaundiced, but there was a mild to moderate degree of leukocytosis. Vegetative forms of *E. histolytica* could not be recovered from the stools of these patients, but cysts were found in the stools in 6 of them. Chest roentgenograms showed elevation of the right leaflet of the diaphragm together with opacity of the empyema in 5 patients and consolidation of the middle and lower lobes in the 3 patients with lung abscess.

Conservative treatment was tried first, using emetine hydrochloride, 60 mg intramuscularly for 5 days, and chloroquine tablets, 600 mg/day for 10 days, together with oxytetracycline or ampicillin, 1 gm/day for 5 days. For patients in poor general condition, metronidazole, 1.2 gm/day, was given for 10 to 14 days instead of emetine hydrochloride. Needle aspiration was done for patients with empyema, but it was not easy and the results were unsatisfactory because of the thick, viscid pus. Intercostal drainage was tried in 3 of these patients, 1 of them with hepatobronchial fistula, but the lung did not expand. For patients with lung abscess postural drainage was encouraged, but no roentgenographic improvement was observed. The pleural aspirate was sterile on culture and positive for vegetative forms of *E. histolytica* in all patients with empyema.

In view of the failure of conservative treatment in patients with pleuropulmonary amebiasis, operation was contemplated. Decortication was carried out in 5 patients with empyema. The parietal as well as the visceral pleurae were quite thick in relation to the relatively short period of contamination, which on the average had been three weeks. When the lower part of the lung was dissected from the diaphragm, a rent in the superior part of the diaphragm leading to the abscess in the right lobe of the liver was found in all 5 patients.

In the patient with hepatobronchial fistula the middle lobe adhered to the liver abscess, and on dissection there was some bronchiolar air leak. After dissection the middle lobe expanded completely on inflation, and thus it was preserved. Four months later a bronchogram showed expansion of the middle lobe and no hepatobronchial communication (Fig 3).

In patients with lung abscess the affected part of the lung was consolidated, and on dissection a communication between the liver abscess and lung through an opening in the diaphragm was found. Lobectomy was done for the affected part of the lung using the standard procedure. His-

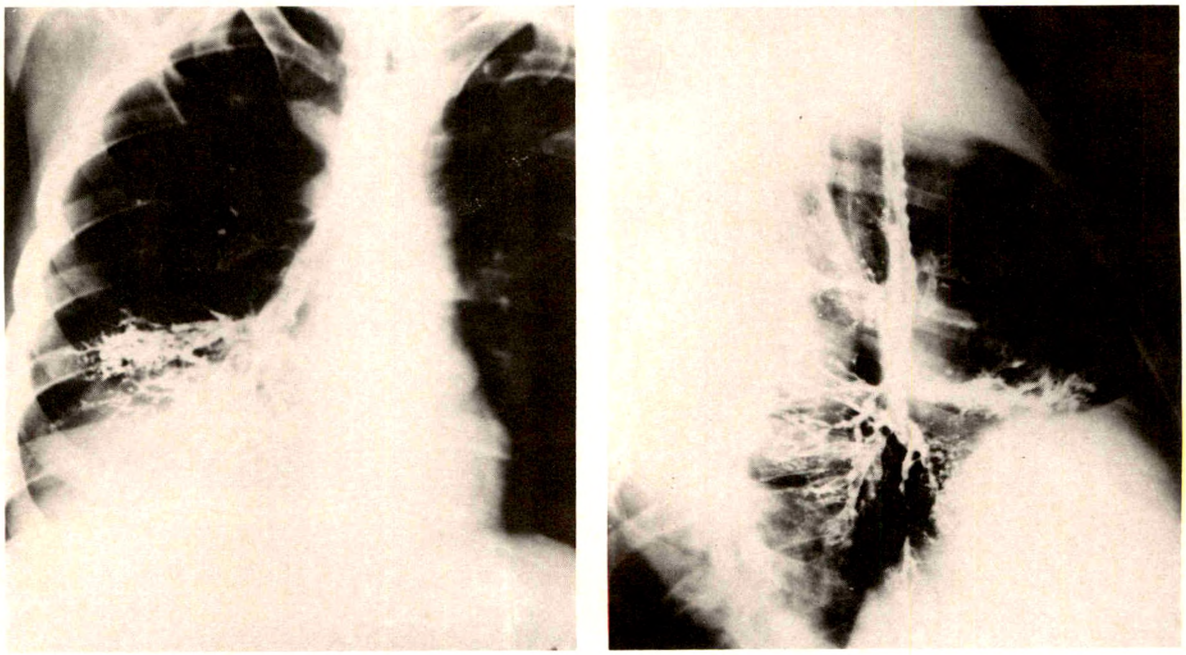

A B

Fig 3. (A) Right bronchogram of the same patient as in Figure 1 four months after decortication operation preserving the middle lobe. (B) Right lateral view of the same patient. Note the full expansion of the middle lobe with no trace of the hepatobronchial fistula. The right leaflet of the diaphragm is still high but much less so than before, and there is no evidence of any diaphragmatic herniation.

tological examination of the lung abscess proved positive for *E. histolytica*. Following decortication or lobectomy, intrapleural drainage of the abscess was instituted. The opening in the diaphragm was widened, and the abscess was removed; its contents were thick and had the appearance of a brownish anchovy sauce. In all the patients with pleuropulmonary amebiasis the liver abscess was solitary and situated in the most superior part of the right lobe of the liver; its diameter ranged from 5 × 2 to 15 × 10 cm. The right leaflet of the diaphragm was found to be adherent to the right lobe of the liver with no subphrenic space. Intercostal drainage was continued for 3 to 5 days after the operation.

In all the patients, antiamebic treatment was continued in the form of metronidazole, 1.2 gm/day for 10 days, and ampicillin, 1.5 gm/day for 5 days. The postoperative period was uneventful, and early chest roentgenograms showed clear lung fields, expansion of the lungs, but a raised right leaflet of the diaphragm.

Intrathoracic Amebic Shadow

A man aged 25 years complained of pain in the right hypochondrium and had a low-grade fever of 37.5°C. Clinical examination of the chest and heart revealed nothing, but his liver was slightly tender. A chest roentgenogram showed a right oval shadow close to the cardiophrenic angle. Blood analyses were within normal limits. He was diagnosed provisionally as having amebic hepatitis and received a full course of emetine hydrochloride and oxytetracycline, but no improvement was seen on subsequent roentgenograms. Further clinical evaluation and screening raised the possibility of an intrapulmonary lesion or a pericardial cyst (Fig 4), and thus right thoracotomy was advised.

Exploration revealed a normal right lung and normal pericardium, but the anterior part of the diaphragm was raised and fluctuant. Aspiration of the typical anchovy sauce pus confirmed the diagnosis of amebic liver abscess bulging into the chest. Because experience has shown that drainage of amebic liver abscess into the pleura is quite safe as long as the patient is on antiamebic treatment, transpleural drainage of the abscess was performed. The elevated part of the diaphragm was thin and stretched. It was incised to about 5 cm in length, and a huge amount of pus, amounting to nearly half a liter, was suctioned out. The abscess was completely re-

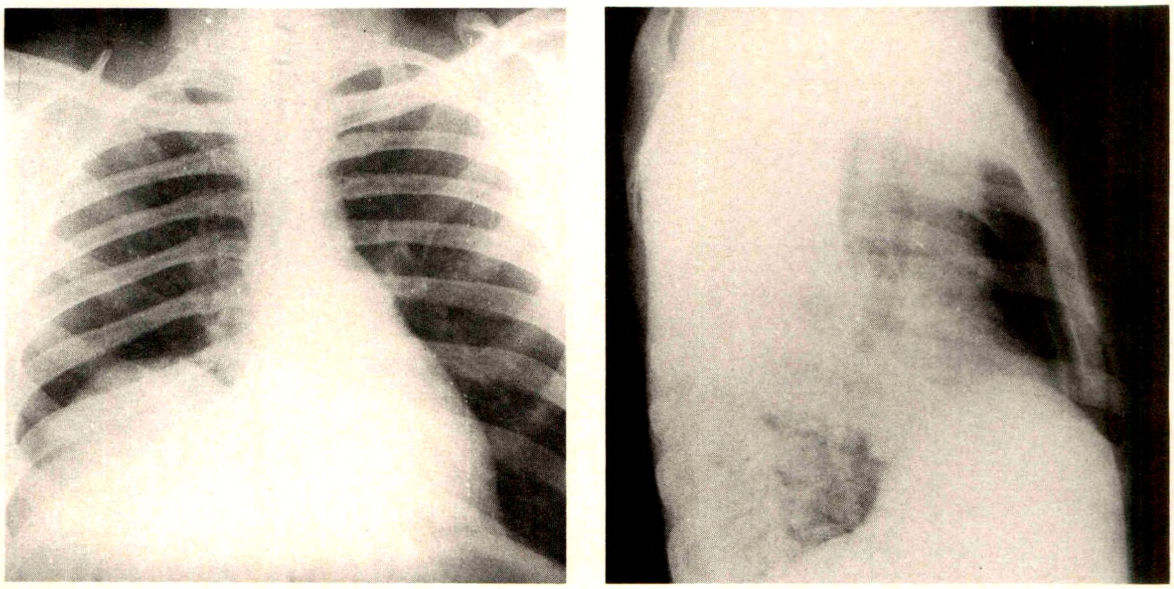


Fig 4. (A) Intrathoracic shadow proved on exploration to be amebic liver abscess in the right lobe of the liver bulging into the chest. The provisional diagnosis was either intrapulmonary lesion or pericardial cyst. Transpleural drainage was done successfully. (B) Right lateral view of the same patient.

moved, and the diaphragm was left open to allow the abscess to drain into the pleural cavity, where the intercostal drain was left for 5 days. The patient had an uneventful recovery. The aspirate was sterile on culture and positive for *E. histolytica*, which was also confirmed by histological examination of the abscess wall. Four weeks later a chest roentgenogram showed clear lung fields, and the right leaflet of the diaphragm was seen to be slightly raised.

Pericardial Amebiasis

A 17-year-old boy had a history of amebic dysentery four years before the present illness. He developed amebic liver abscess of the left lobe of the liver and received a full course of emetine hydrochloride and ampicillin with marked regression in the size of the liver abscess. A few days later his general condition deteriorated, with dyspnea, orthopnea, and an increase in cardiac dullness. His temperature was 37.7°C, and he had a paradoxical pulse of 110 per minute, blood pressure of 70/50 mm Hg, and cold extremities, peripheral cyanosis, and engorged neck veins—the picture of cardiac tamponade. The chest roentgenogram showed globular enlargement of the heart shadow and raised left diaphragmatic copula with right pleural effusion (Fig 5A). The total leukocyte count was 11,000 per mm^3 with 75% polymorphonuclear leukocytes, and the electrocardiogram showed a low-voltage QRS complex in the limb and chest leads. Repeated pericardial aspirations were done below the xiphoid process, and amounts ranging between 250 and 500 ml of typical amebic pus were withdrawn that proved sterile on ordinary culture and positive for the vegetative forms of *E. histolytica*. Pleural aspiration was done concomitantly twice and yielded 700 and 500 ml, respectively, of straw-colored fluid that was sterile on culture.

About three weeks from the start of the disease the patient's liver returned to normal size, but his neck veins were still engorged and the cardiac size did not show any improvement on roentgenogram. His general condition remained poor. These clinical changes were explained by the development of pericardial constriction, and we decided to perform a pericardiectomy.

Through a left anterolateral thoracotomy incision, the pericardium was found to be tense and full of fibrinous clots. It was excised entirely from the left ventricle and from most of the right side. The pericardium was quite thick in relation to the fairly short duration of the disease, reaching 4 mm in thickness in some parts. The

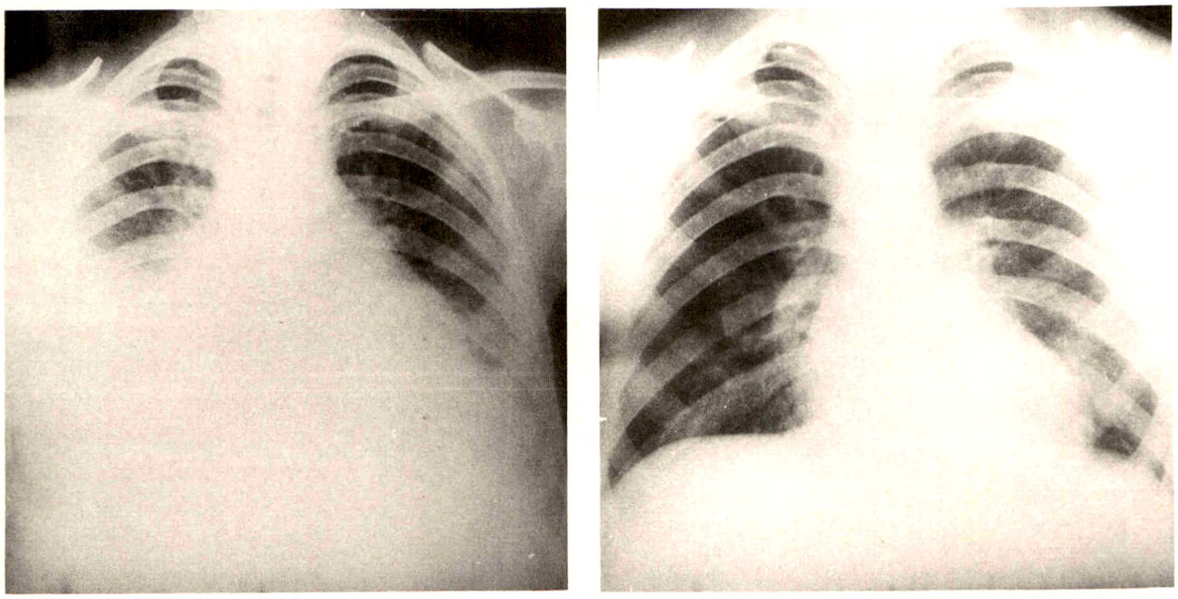


Fig 5. (A) Amebic pericarditis. Note the globular enlargement of the heart, the right pleural effusion, and the raised left leaflet of the diaphragm. (B) Two months after pericardiectomy. Note the normal cardiac size, the clear lung fields, and the normal level of the left leaflet of the diaphragm.

epicardium was covered by a thin layer of fibrin that interfered with the cardiac action. There was no trace of any communication between the pericardium and the left lobe of the liver or any structure below the diaphragm, which may be explained by the fact that by the time of the operation the liver abscess had healed completely. Histological examination of the pericardium showed chronic, nonspecific inflammation and organization of granulation tissue at various stages of maturation.

The patient had an uneventful recovery and received metronidazole, 1.2 gm/day, and ampicillin, 1.5 gm/day, for one week. Two months after the operation the patient had returned to normal activities and his chest roentgenogram showed a normal-sized heart and clear lung fields (see Fig 5B).

Follow-up

All the patients in this series were followed from two to eighteen months after operation with no mortality or morbidity. On roentgenograms the lung fields were clear and the diaphragm was found to be raised with no evidence of herniation of the liver through the diaphragmatic defect created for the transpleural drainage of the liver abscess. It takes some time for the diaphragm to regress to its normal level.

Comment

Intrathoracic amebiasis is a serious complication of amebic liver abscess which commonly affects the right lobe of the liver [2, 4, 9] and thus explains the frequent involvement of the right side of the chest. *Entamoeba histolytica* finds its way directly to the thorax through the diaphragm by its lytic action, which erodes the diaphragm. Infection borne through the blood or the lymphatics may explain pulmonary involvement in parts of the lungs which are not directly related to the diaphragm or in patients with no evident hepatic involvement [3, 8]. Diffuse amebic hepatitis or small amebic abscesses can be controlled by antiamebic treatment, but large abscesses with copious amounts of pus cannot be cured by conservative means alone. Such liver abscesses are the source of the pleuropulmonary complications. The development of intrathoracic involvement, either pleural or pulmonary, depends on the pleural cavity and whether it is obliterated by or free from adhesions [9]. If there are adhesions, once the liver abscess bursts through the diaphragm it can find its way into the parts of the lungs related to the diaphragm—ie, the middle lobe or the lower lobe on the right side—whereas if there are no pleural adhesions, the abscess will open easily into the pleural cavity. In either case, if the pus is under tension, it can find its way through the bronchi, giving rise to hepatobronchial fistula. This is a serious complication, as secondary infection may occur or spill over to the other lung [3, 9, 10].

Once *E. histolytica* reaches the serous membranes of the pleura or the pericardium, it creates a severe reaction, producing thickening of these membranes out of proportion to the duration of contamination, which is a matter of weeks rather than months. This picture is quite different from that presented by nonspecific or other specific inflammatory processes such as tuberculosis. This early thickening of the pleura in patients with empyema prevents lung expansion and enhances the cardiac constriction in amebic pericarditis, which is exacerbated by the viscid nature of the amebic pus. These factors together explain the failure of conservative treatment in patients with intrathoracic amebiasis. We have found that transpleural drainage of amebic liver abscess is safe provided it is done concurrently with adequate antiamebic treatment. The transthoracic approach also gives direct access to the liver abscess.

Amebic pericarditis is a rare complication. Its incidence is 0.2 to 2.8% among patients with amebic liver abscess [6]. Up to January, 1975, 81 cases of amebic pericarditis had been reported [5], most of them secondary to amebic abscess of the left lobe of the liver. There are just a few reports of amebic pericarditis resulting from the extension of abscesses in the right lobe of the liver or from amebic lung abscess [9, 11].

Amebic pericarditis can be seen in two stages: the presuppurative stage and the suppurative stage. The first stage is sometimes termed the reactive or sympathetic stage [5]. All patients in this stage of amebic pericarditis should be viewed as likely to develop advanced suppurative pericarditis. Conservative treatment in the form of antiamebic treatment and proper pericardial aspiration, if needed, yields a recovery rate of 60%, provided it is started early [7]. The average mortality rate from amebic pericarditis is 40% [5]. If the patient does not improve with conservative treatment, one should consider pericardial constriction. Once this complication develops, pericardiectomy is indicated. In advanced cases there will be liver damage because of chronic venous congestion as well as the possibility of myocardial damage caused by the spread of fibrosis.

We concluded that to prevent the serious complication of intrathoracic amebiasis, large amebic liver abscesses that are unlikely to be controlled by conservative treatment can be drained from the chest by opening the right leaflet of the diaphragm, aspirating the contents, and breaking down any septa in the abscess cavity. This allows adequate drainage into the pleura, where an intercostal drain is placed. In our patients there were no complications from incising the right leaflet of the diaphragm and leaving it open for drainage because of the dense adhesions already present between the diaphragm and liver. Intrapleural drainage of the amebic liver abscess did not lead to any complications in the early or late postoperative period as long as adequate antiamebic treatment was given. Early operation is indicated, particularly in patients with hepatobronchial fistula and also in patients with amebic pericarditis once constriction develops.

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C[illegible]E REPORT

Bypass of Superior Vena Cava with Spiral Vein Graft

Donald B. Doty, M.D., and William H. Baker, M.D.

ABSTRACT **The superior vena cava was successfully bypassed in a patient with superior vena cava syndrome due to granulomatous mediastinitis. A spiral vein graft constructed from autogenous vein was utilized. Complete relief of symptoms and graft patency documented by venography six months after the operation confirm the usefulness of this procedure in patients with superior vena cava obstruction.**

Benign or malignant obstruction of the superior vena cava may cause an extremely disabling syndrome. Treatment of the primary disease process by medical means or radiation therapy, which leads to great discomfort due to venous hypertension in the head and upper extremities, may not relieve the obstruction in the vena cava. Usually the extremity swelling can be accepted, but symptoms of cerebral swelling are poorly tolerated.

This report describes bypass of the superior vena cava obstructed by granulomatous mediastinitis in a patient with disabling cerebral symptoms of superior vena cava syndrome. A spiral vein graft, constructed from the patient's own saphenous vein after the method described by Chiu, Terzis, and MacRae [1], was used to connect the innominate vein and the right atrial appendage.

A 49-year-old man was admitted to the University of Iowa Hospitals with superior vena cava syndrome. He was a farmer and was unable to work because the slightest exertion on bending forward produced dizziness, lightheadedness, and near syncope. Recent plethora, puffiness of the face, and swelling around the eyes had been noted. Physical examination showed moderate swelling of the face, periorbital edema, conjunctival injection, and distended external jugular veins. Laboratory studies were noncontributory. Skin tests for tuberculosis and *Histoplasmosis* were positive. Chest roentgenograms showed a mass on the right side in the mediastinum. Biopsy of right scalene lymph nodes was not diagnostic.

An exploratory thoracotomy revealed a firm, fixed mass in the mediastinum on the right side. The superior vena cava and azygos vein were involved in the disease process. Both great veins were evidently thrombosed. An incisional biopsy of the mediastinal mass was performed; lymph nodes with caseous necrosis were encountered. A portion of the adjacent right upper lobe of the lung, which also appeared to be involved, was excised using an autosuture stapling device. Histopathologically the biopsy specimen revealed granulomatous inflammation with caseous necrosis. No causative organism could be identified, and microbiology cultures revealed no growth. Inoculation studies were negative.

The patient's convalescence was uncomplicated, but the symptoms of superior vena cava syndrome were not relieved. He was unable to work, and even the slightest exertion produced great discomfort. Antituberculous medical therapy was administered for one year. During this time it was hoped that sufficient venous collateral channels would develop to relieve the symptoms of cerebral venous hypertension. Both the disease process and the resultant symptoms, however, were static.

The patient was readmitted one year after the initial exploratory thoracotomy. Venography was performed by injection of contrast medium into the basilic veins bilaterally and demonstrated obstruction of the superior vena cava, azygos vein, and innominate vein. The large collateral veins that had developed were all to the hemiazygos venous system and apparently were inadequate to decompress the head veins (Fig 1). Operation to bypass the superior vena

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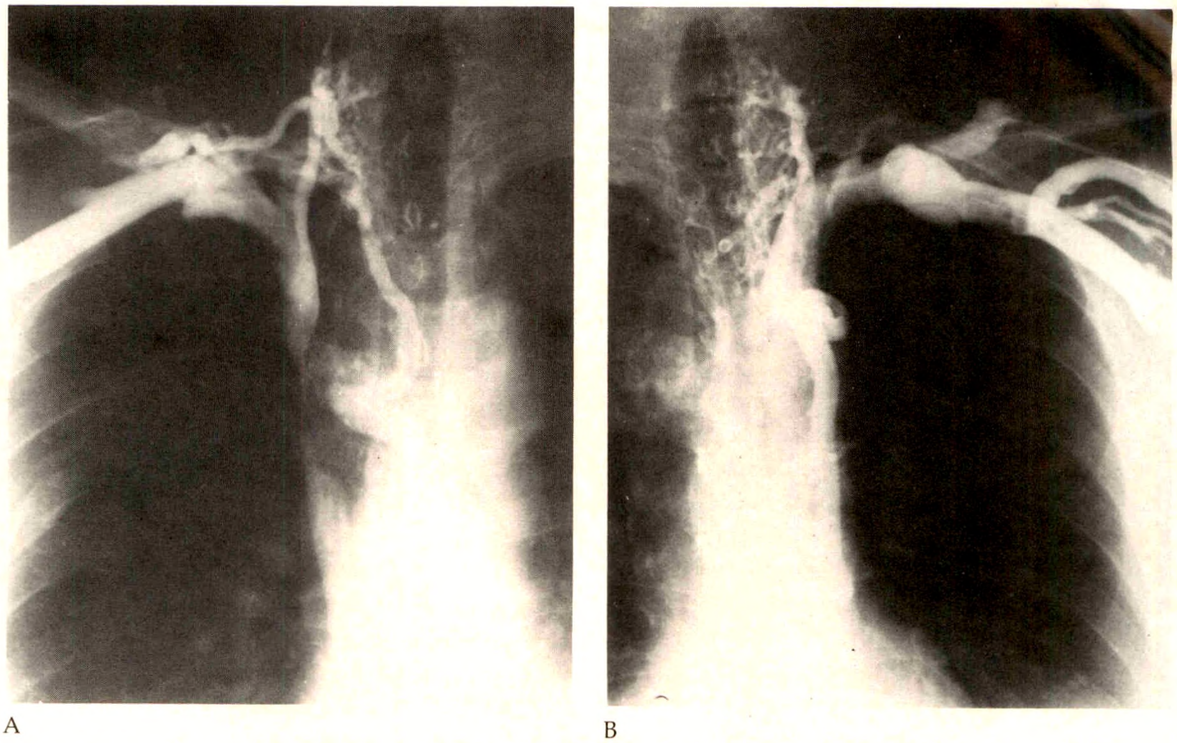

Fig 1. Preoperative venograms show obstruction of the superior vena cava and innominate vein, with collateral veins to the hemiazygos system. A row of staples from the previous biopsy procedure is seen adjacent to the venous obstruction.

cava was elected. Since all symptoms were related to cerebral venous hypertension, it was reasoned that because the cerebral veins are confluent at the cavernous sinus, decompression of one internal jugular vein would suffice.

A midsternal incision was made, the thymic remnant was removed, and the upper portion of the pericardium was opened to expose the right atrial appendage. The superior vena cava and innominate vein were found to be thrombosed. The distance from the confluence of the left internal jugular and left subclavian veins to the right atrial appendage measured 7 cm. A simultaneous incision was made in the left thigh over the course of the greater saphenous vein. It was decided to construct a spiral vein graft 10 mm in diameter; this was approximately the diameter of the left internal jugular vein. The saphenous vein was about 5 mm in diameter. Using the formula $l = R/r \times L$ where R = radius of recipient vessel, L = length of recipient vessel, r = radius of donor vessel, and l = length of donor vessel, it was determined that 14 cm of saphenous vein was required. The sidebranches were ligated, and the vein was tested for leakage and then opened longitudinally. A 28F Argyle catheter (9.5 mm diameter) was used as a stent, and the vein was wrapped in a spiral fashion. The edges of the vein were sutured together using a running stitch of 7-0 Prolene (Fig 2). Optical loupe magnification was used throughout the procedure to ensure accuracy of anastomosis and that no extraneous material was included in the suture lines.

Heparin, 5,000 units, was administered. The innominate vein was divided distal to the thrombosed portion, and the completed spiral vein graft was anastomosed to the confluence of the left jugular and subclavian veins using 7-0 Prolene. The spiral graft was then attached to the right atrial appendage, which was isolated using an exclusion clamp. The completed bypass graft assumed an unobstructed position in the anterior mediastinum (Fig 3).

The hospital convalescence was not complicated. Dipyridamole, 100 mg per day, and aspirin, 600 mg per day, were administered orally. The patient noted immediate relief of symptoms and soon returned to full-time farming with no restrictions. The plethora completely disap-

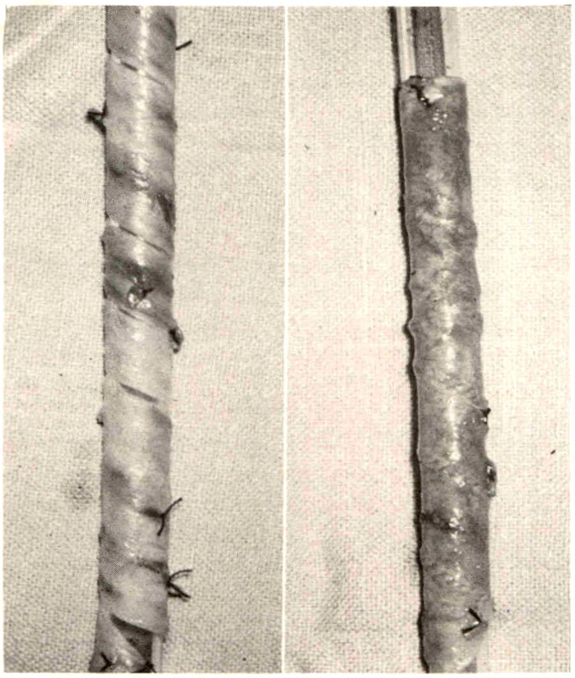

Fig 2. The spiral vein graft is constructed from longitudinally opened saphenous vein wrapped around a tubular stent (left). *The graft is completed using a continuous stitch of fine monofilament suture* (right).

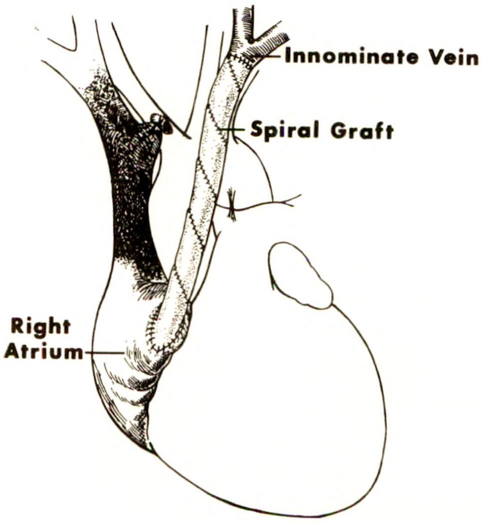

Fig 3. The operation. The junction of the left internal jugular and subclavian veins is anastomosed to the spiral vein graft. Anastomosis of the graft to the right atrium completes bypass of the obstructed superior vena cava.

peared, but slight external jugular venous distention persisted. Examination of the left internal jugular vein using Doppler techniques showed increased venous flow compared with the right side. Venograms were performed one week and six months after operation by injecting the left basilic vein with contrast medium. Graft patency was documented. Opacification of the graft was somewhat reduced by high-volume admixture of nonopacified blood from the left internal jugular vein (Fig 4). The patient was asymptomatic eighteen months after operation.

Comment

Clinical features of superior vena cava obstruction as they relate to the anatomical site of obstruction have been reviewed by Gomes and Hufnagel [2]. They found that when both the superior vena cava and azygos vein are obstructed, as in this case, collateral veins are especially prominent and venous pressure is

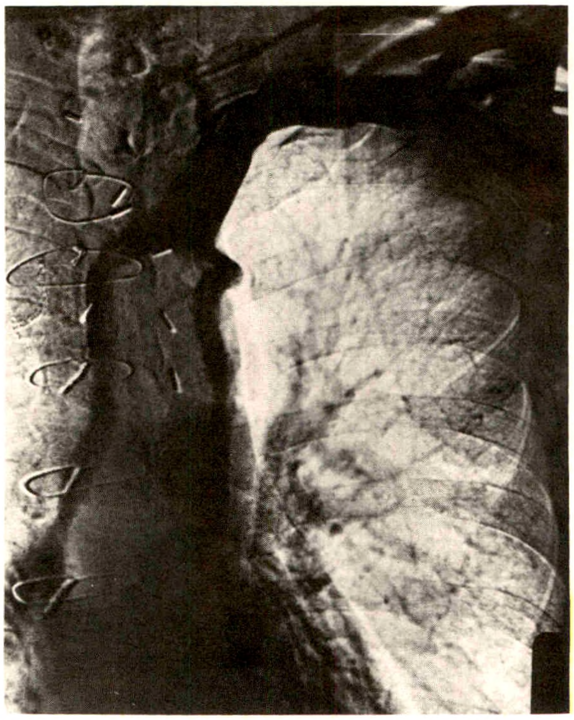

Fig 4. Postoperative venogram (subtraction technique) demonstrates patency of the spiral vein graft. Contrast in the graft is slightly diminished due to admixture of nonopacified blood from the left internal jugular vein. Note the adjacent hemiazygos collateral vein, also seen in the preoperative study.

elevated. Generally, collateral channels become sufficient with time so that they are able to shunt blood around the obstruction, thus avoiding major symptoms under basal conditions. In this patient, however, the slightest exertion still produced severe symptoms one year after onset and prevented gainful occupation, so that decompression of the cerebral venous system beyond the degree provided by collateral circulation appeared warranted.

The current status of vena cava replacement has been reviewed by Scherck, Kerstein, and Stansel [4]. They stated that replacement of venous segments has not been successful enough to be applied in any but the most desperate of clinical situations. A number of factors are responsible, and it seems apparent that autogenous venous grafts of nearly the same size as affected vein are most likely to remain patent. Taylor and associates [5] have shown that long segments of saphenous vein are sufficient to decompress the obstructed superior vena cava through bypass to the groin. The technique of Chiu, Terzis, and MacRae [1] showed much promise experimentally and has the advantage of utilizing autogenous saphenous vein plus the versatility of producing a graft of predictable diameter and length so that size discrepancies are eliminated.

The patient was given dipyridamole and aspirin to reduce platelet adhesiveness, based on experimental studies of Hasegawa and associates [3] in prosthetic replacement of the superior vena cava. This medical adjunct to a new and useful operative technique produced an excellent clinical response in the difficult syndrome of obstructed superior vena cava.

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Editor's Note

The superficial femoral vein can be used to bypass the superior vena cava (Skinner et al, J Thorac Cardiovasc Surg 49:824, 1965). A member of The *Annals* Editorial Board reports having used the superficial femoral vein to bypass the superior vena cava successfully in 3 patients.

NOTE

A New Instrument for Measurements in Cardiovascular Surgery

James S. Donahoo, M.D., and Eoin Aberdeen, F.R.C.S.

ABSTRACT **An instrument for performing measurements in cardiac and vascular operations is described. This device is a modification of a vascular clamp that provides an accurate and simple method for making intracardiac measurements. The instrument is constructed to provide easy readout of even extremely small measurements.**

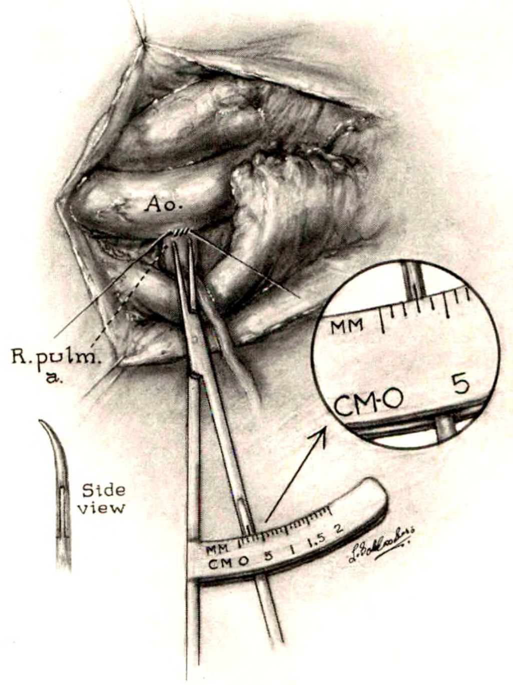
In performing cardiovascular surgical procedures, it frequently benefits the surgeon to make accurate measurements of lesions, vessel diameters, and lengths of suture line. The need for this accuracy is nowhere better demonstrated than in the construction of a systemic–pulmonary artery shunt in very small children, in whom the suture line measurement can be critical. We have found many of the currently available measuring devices to be clumsy and not truly designed for this particular purpose. We present here an instrument that facilitates measurements in cardiovascular operations and increases their accuracy.

Description and Clinical Use

The instrument is a modification of a long vascular clamp (Figure). The tips are constructed so as to make fine measurements possible even in relatively inaccessible areas. The clamp is long enough to permit almost any area of the chest or heart to be measured readily. The calibration scale is located well up the handle of the instrument, which provides for more accessible readout of measurements. Because the joint of the clamp is located close to the tip, there is a 50% augmentation of the actual distance on the caliper, allowing for easier readout. This is especially helpful when very small measurements, down to 1 or 2 mm, are needed.

We have used this instrument to measure the lengths of suture lines (see the Figure), the internal diameter of cardiac defects, and the diameter of intracardiac and extracardiac vessels. It has also been helpful in fashioning appropriate-sized patches and selecting the correct size vascular prosthesis.

The instrument being used to measure a Waterston shunt. Note the augmentation of the actual measurement on the caliper. (Ao. = *aorta.)*



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Palliation of Infants with Truncus Arteriosus through Creation of a Pulmonary Artery Ostial Stenosis

J. Jacques Mistrot, M.D., Richard L. Varco, M.D., and
Demetre M. Nicoloff, M.D.

ABSTRACT **A surgical procedure for palliation of infants with truncus arteriosus and excessive pulmonary blood flow (types I, II, and III) is described. The technique involves the production of ostial stenosis of the pulmonary artery from within the truncus using cardiopulmonary bypass. This method has been employed in 2 infants. The technique has advantages over pulmonary artery banding, which in general has produced disappointing results.**

Corrective operation is now available for all three types of truncus arteriosus if the pulmonary vascular resistance is appropriate and if the child is large enough [2, 5]. Although this same procedure has been utilized in infancy, the conduit that can be used at this age will surely not be large enough later in life. Ideally, a palliative procedure would uniformly: (1) decrease pulmonary flow, (2) prevent congestive heart failure, (3) prevent development of pulmonary hypertensive vascular changes, (4) preserve the pulmonary arteries so that future correction would not be complicated, and (5) carry a low morbidity and mortality.

Technique

A median sternotomy is used. The ascending aorta is cannulated just proximal to the origin of the innominate artery, the right atrium with one cannula in the right atrial appendage. Cardiopulmonary bypass is begun and systemic hypothermia to 30°C is employed. The aorta is cross-clamped and a transverse incision is made in the truncus. The pulmonary artery ostium is narrowed with interrupted sutures and calibrated to a diameter of 4 to 5 mm in types I and II or 3 mm each in type III (Figure). For calibration a Hegar dilator is used. The incision is closed; air is vented from the aorta and bypass is terminated following rewarming.

Patient 1

A 3 kg infant developed heart failure at 1 week of age. Catheterization revealed type 1 truncus arteriosus. In spite of intensive medical management the child continued to do poorly, and operation was advised at 4 weeks of age. At operation the pulmonary ostium, which was found to be 12 mm in diameter, was narrowed to 5 mm (Figure, *1*). Total bypass time was 18 minutes with an aortic cross-clamp time of 12 minutes. Postoperatively the child showed marked clinical improvement, with increased pulmonary compliance and decreased signs of heart failure.

Thirty hours postoperatively, two hours following intravenous administration of digitalis, the child developed atrioventricular dissociation, arrested, and could not be resuscitated. Postmortem examination showed both lungs to be normal. No anatomical explanation was found for the cause of death.

Patient 2

A 2½-month, 2,900 gm infant was admitted in severe congestive heart failure. Angiography revealed a type III truncus arteriosus, and because of increasing congestive heart failure on maximal medical therapy, the patient was operated upon. Utilizing cardiopulmonary bypass, the 6 mm separate pulmonary artery ostia were narrowed to 3 mm each (Figure, *3*). Total bypass time was 28 minutes with an aortic cross-clamp time of 12 minutes.

The patient tolerated the procedure well and showed marked clinical improvement postoperatively. Mechanical ventilation, which had

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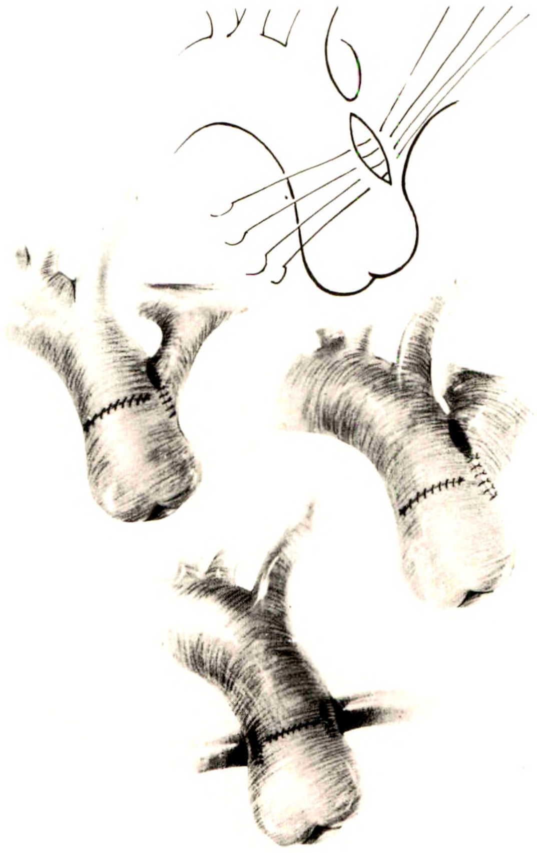

Surgical procedure used in treatment of the three types of truncus arteriosus.

been instituted preoperatively because of pulmonary edema, was discontinued twenty-four hours after the operation. The patient was discharged two weeks postoperatively with normal heart size, normal pulmonary vasculature by chest roentgenogram, and no signs or symptoms of congestive heart failure.

Comment

Since a successful operation for correction of truncus arteriosus was developed, the outlook for children affected by this defect has greatly improved [5]. The major problem that remains is getting these infants to appropriate size (age 5 to 12 years) without prior development of significant pulmonary arterial obstructive disease. The majority of infants with truncus arteriosus die in infancy, and a substantial number of patients who survive infancy are not acceptable candidates for repair because of pulmonary hypertension. The operative mortality for corrective operation in the presence of significant pulmonary hypertension is 60%; it is 17% when the pulmonary-to-systemic pressure ratio is less than 0.6 [5]. The long-term success of correction, as well as the operative mortality, appear to depend upon delaying the operation until the age of 5 or older. This allows the use of a pulmonary conduit that will be of adequate size for adulthood and entails a lower operative mortality [5]. Because of the need for delay, however, an early palliative decrease in pulmonary blood flow is mandatory.

The results of pulmonary artery banding for this defect have been disappointing. First, the operative mortality has been 75% or higher [1–3, 6, 8]. Second, pulmonary arteries must be banded separately in types II and III and in most cases of type I truncus. Banding one of the pulmonary arteries has been unsuccessful [3]. Third, the posterior position of the pulmonary arteries requires banding through a median sternotomy approach. Finally, difficulties associated with removal of the bands and any pulmonary artery reconstruction at the band site prolong the operative time on cardiopulmonary bypass and require that the anastomosis be made distal to the site of pulmonary band placement in a smaller pulmonary artery, which could be an immediate or a future point of pulmonary stenosis because of the size of the vessel involved. (Experience with pulmonary artery debanding indicates that nearly 50% of these patients will require pulmonary angioplasty [4].) Although one would expect the mortality to be higher in nonbanded patients than in those with bands, studies from the Mayo Clinic do not show this to be the case [7]. Whether this is true in other centers is not presently known.

Because of these results and technical problems associated with pulmonary artery banding in truncus arteriosus, we propose a technique that creates ostial stenosis of the pulmonary artery (type I) or arteries (types II and III) from within the truncus using cardiopulmonary bypass. It has been carried out in 2 infants (types I and III). Though the first died thirty hours postoperatively, the death did not appear related to the operative procedure, and clinical signs of failure had resolved. It seems likely that the death was related to digitalis toxicity. The second infant has done well, shows no evidence of failure, and is gaining weight.

The technique of creating ostial stenosis has certain theoretical advantages over pulmonary artery banding in truncus arteriosus. With this procedure, accurately calibrated narrowing of the internal diameter of the pulmonary artery can be performed. Our experience with pulmonary artery banding in infants with ventricular septal defect has shown that a band with a circumference of 27 to 28 mm produces excellent results. From the thickness of the pulmonary artery wall and the crimping effect of banding, we estimate that a pulmonary artery internal diameter of approximately 4 to 5 mm is created. In addition, experience with ascending aorta–pulmonary artery shunts in infants suggests that a 4 to 5 mm anastomosis is well tolerated. Therefore, we have used this ostial stenosis diameter in types I and II and 3 mm for each of the pulmonary artery ostia in type III. (The cross-sectional area of two 3 mm ostia is approximately equal to that of one 4 mm ostium.) Placing sutures in only one segment of the ostial circumference as shown in the Figure may allow growth of the remaining segment with age. This may obviate the need for a later systemic–pulmonary shunt, which might be required if a rigid pulmonary band were used to limit the cross-sectional area of the vessel.

Although we have not yet done a corrective procedure following palliation with this technique, we anticipate that certain benefits will be derived: (1) no bands will have to be removed, (2) no pulmonary angioplasty will be necessary, (3) in type I and II truncus only one distal anastomosis will be necessary, and (4) the distal anastomosis will be done in a large, proximal, accessible vessel rather than in a smaller distal vessel. Correction using a prosthetic conduit during infancy has been done successfully. However, because of the size of the conduit there is no doubt that a future operation will be necessary. The combined mortality and morbidity of these two procedures will determine which is the preferred method of treatment.

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A Further Look at Tricuspid Annuloplasty

Jerome Harold Kay, M.D., A. Michael Mendez, M.D., and Pablo Zubiate, M.D.

ABSTRACT **Is it necessary to replace the tricuspid valve or insert a tricuspid ring for pure tricuspid insufficiency, or is repair satisfactory? In 96 of 113 patients with pure tricuspid insufficiency the tricuspid valve was repaired by converting the incompetent three-leaflet valve into a two-leaflet one. To avoid liver damage in these critically ill patients, the inferior caval tie was omitted during the open-heart procedure. There have been 5 deaths in the last 51 consecutive operations. Three patients developed recurrent tricuspid insufficiency secondary to failure of the mitral repair or replacement. It is concluded that tricuspid repair for pure tricuspid insufficiency is a simple and excellent method for treating severe, pure tricuspid insufficiency.**

An article entitled "Surgical Treatment of Tricuspid Insufficiency" [4], published in 1965, described our early experience with 20 patients in whom the mitral valve was repaired or replaced and the tricuspid valve repaired for severe secondary tricuspid insufficiency. There were 6 operative deaths among these 20 patients. The patients who died had an excellent repair of the tricuspid valve but died either from liver failure with marked jaundice and hepatic necrosis around seven to ten days postoperatively or from pulmonary insufficiency associated with the pronounced pulmonary hypertension.

Pluth and Ellis [5] in 1969 and Boyd and colleagues [1] in 1974 published articles on tricuspid valve disease. Carpentier and his associates [2] in 1971 described a reconstructive operation, employing a ring, for correction of mitral and tricuspid insufficiency. In 1975 Grondin and co-workers [3] reported on their results using the Carpentier method.

Our technique of annuloplasty for tricuspid insufficiency has not varied since 1961. The method is simple and consists of converting an incompetent three-leaflet valve into a competent two-leaflet one. All the suturing must be done in such a fashion as to do away with the posterior leaflet. This technique approximates the large anterior leaflet to the septal leaflet. Two or, at most, three figure-of-eight sutures of No. 2 silk are placed in the annulus of the posterior leaflet. Starting at the midportion of the annulus of the posterior leaflet, a figure-of-eight suture is taken from the outside of the annulus to the inside. This suture then goes from inside to outside. With this same suture the next stitch is taken slightly lateral to the first stitch from outside to inside. This suture is then completed by taking the next stitch from inside to outside. A similar suture is placed on either side of the previous stitches until the commissure between the anterior and posterior leaflets has been approximated to the commissure between the septal and posterior leaflets. This decreases the annulus from a four or five fingerbreadth opening to a loose, two fingerbreadth opening (Fig 1). If done correctly, a two-leaflet valve is created. There is no danger of producing complete heart block since the suturing is performed away from the area of the atrioventricular node and the conduction system.

Until 1968 the surgical mortality continued to be high. The patients died of liver necrosis within a week or two after operation or else of pulmonary hypertension. The majority of these patients with tricuspid insufficiency were severely ill preoperatively because of longstanding pulmonary hypertension or failure and secondary cardiac cirrhosis of the liver. It was reasoned that with an inferior caval catheter in place, drainage through the inferior cava might not always be adequate, thereby producing an increase in pressure in the vessel. This increased pressure would be reflected back into the cirrhotic liver, with pressure on the liver cells against the firm, scarred latticework causing destruction of the cells.

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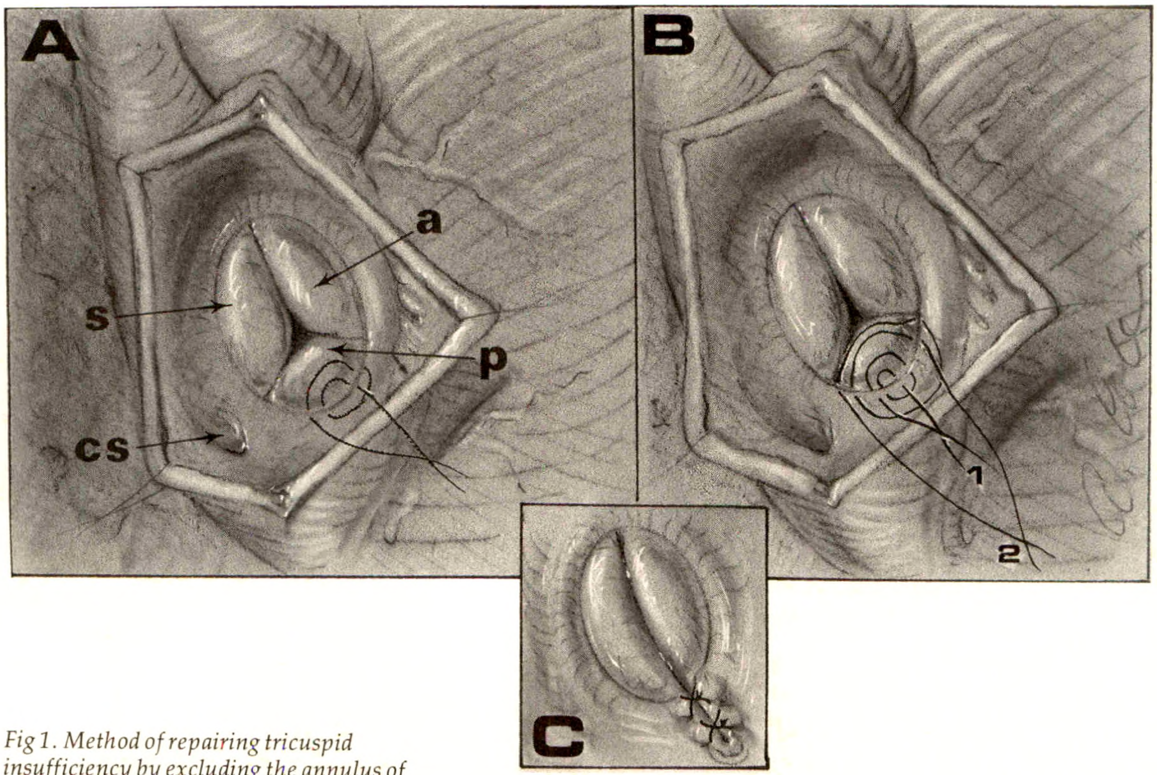

Fig 1. Method of repairing tricuspid insufficiency by excluding the annulus of the posterior leaflet. (s = *septal leaflet;* a = *anterior leaflet;* p = *posterior leaflet;* cs = *coronary sinus.)*

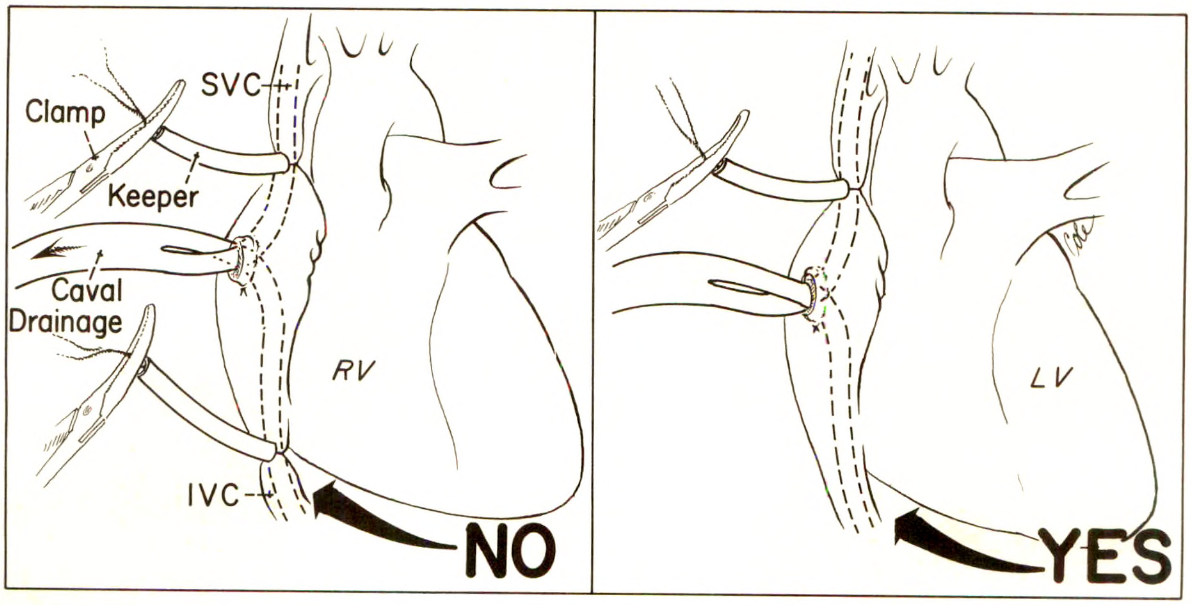

Fig 2. An inferior caval tie must not be employed in operations on the mitral or tricuspid valve. (Left) *Incorrect: superior and inferior caval ties.* (Right) *Correct: superior caval tie only.* (SVC = *superior vena cava;* RV = *right ventricle;* IVC = *inferior vena cava;* LV = *left ventricle.)*

Since 1968, superior and inferior caval ties have not been employed for any patients undergoing mitral valve operations. If the tricuspid valve is to be repaired, only a superior caval tie is used (Fig 2). The tip of the inferior caval catheter is inserted through an incision in the right atrium and down the inferior vena cava for a distance of 7.5 to 10 cm below the diaphragm. After the incision in the right atrium is made to repair the tricuspid valve, two or three suction tubes are placed in the mouth of the inferior cava to maintain a bloodless field while the tricuspid valve is repaired. The correction requires only 3 to 4 minutes, and another 2 or 3 minutes suffices to close the right atrium.

The 96 patients had mitral valve repair or replacement, and 14 had concomitant aortic repair or replacement as well. There were 20 hospital deaths (21%) in this group of 96 patients, 6 of them (30%) in the original 20 patients. Since we began omitting the inferior caval tie in 1968, there have been only 5 deaths among 51 patients (10%). Fifteen late deaths have occurred in 76 patients discharged from the hospital (Table). The actuarial curve reveals a 64% chance of survival at twelve years (Fig 3).

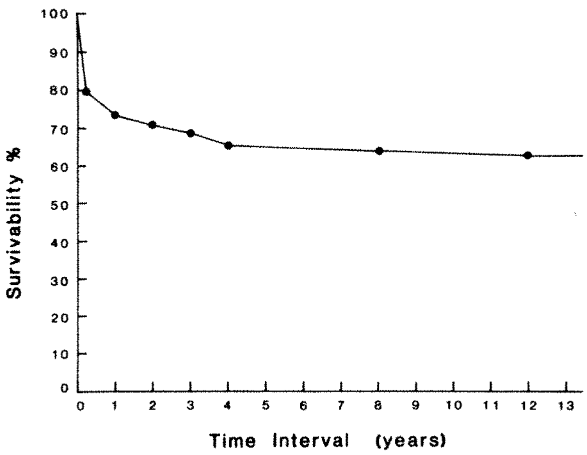

Fig 3. Actuarial curve for long-term survival after tricuspid annuloplasty.

None of the 20 patients who died in the hospital after their operation had tricuspid insufficiency. Three of the 76 patients discharged home had recurrent tricuspid insufficiency, but it was due to recurrence of the underlying mitral valve disease or malfunctioning of the previously replaced mitral valve.

Cause of 15 Late Deaths after Tricuspid Annuloplasty

Cause of Death	No. of Patients
Arrhythmia	1
Coronary artery disease	3
Liver failure	2
Carcinoma	1
Unknown	3
CVA (prosthetic mitral valve)	5

CVA = cerebrovascular accident.

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ELEVENTH POSTGRADUATE PROGRAM
THE SOCIETY OF THORACIC SURGEONS

Sunday, January 23, 1977
San Francisco Hilton Hotel, San Francisco, CA

8:00–11:50 **Morning Session**
Cardiac Valve Surgery—1977

Chairmen W. Gerald Rainer, M.D., Denver, CO, and Jay L. Ankeney, M.D., Cleveland, OH

Evaluation of Prosthetic Heart Valves
Richard E. Clark, M.D., St Louis, MO

Ultrastructure and Critical Evaluation of Tissue Valves
William W. Angell, M.D., San Jose, CA

Reconstructive Valve Surgery: A Critical Review
Clarence S. Weldon, M.D., St Louis, MO

Complications of Valve Replacement: Prevention and Management
George J. Magovern, M.D., Pittsburgh, PA

Review of Valve Surgery of the Past 17 Years
Frank L. A. Gerbode, M.D., San Francisco, CA

Discussion

Lung Cancer—1977

Chairmen Martin F. McKneally, M.D., Albany, NY, and Timothy Takaro, M.D., Asheville, NC

Diagnosis and Evaluation of Lung Cancer
W. Spencer Payne, M.D., Rochester, MN

The Immunology and Immunotherapy of Lung Cancer
E. Carmack Holmes, M.D., Los Angeles, CA

Discussion

1:30–5:30 **Afternoon Session**
Pulmonary Insufficiency—1977

Chairmen Harvey W. Bender Jr., M.D., Nashville, TN, and Theodore R. Sadler, Jr., M.D., Denver, CO

Medical Evaluation and Management
Philip C. Hopewell, M.D., San Francisco, CA

Surgical Evaluation and Management
J. Donald Hill, M.D., San Francisco, CA

Discussion

Pacemakers—1977

Chairmen Clement A. Hiebert, M.D., Portland, ME, and Victor Parsonnet, M.D., Newark, NJ

Measurement of Myocardial Potentials and Stimulation Thresholds
Nicholas P. D. Smyth, M.D., Washington, DC

Pacemaker Follow-up: Practical and Otherwise
William S. Stoney, M.D., Nashville, TN

New Advances: Leads and Lead Placement
Seymour Furman, M.D., Bronx, NY

Power Sources
G. Frank O. Tyers, M.D., Hershey, PA

Complications: Prevention and Management
W. Gerald Rainer, M.D., Denver, CO

Discussion (to be opened by Dr. Parsonnet)

This program is sponsored by the Committee on Postgraduate Education of The Society of Thoracic Surgeons in conjunction with the Thirteenth Annual Meeting.

Registration ($20 fee includes luncheon) is open to all thoracic surgeons and residents. Details regarding registration will be mailed to members; others should write to the Secretary, Thomas D. Bartley, M.D., The Society of Thoracic Surgeons, 111 E Wacker Dr, Chicago, IL 60601.

This program is authorized for eight hours' credit toward the Physicians' Recognition Certificate of the American Medical Association.

PROGRAM
FOR THIRTEENTH ANNUAL MEETING OF THE SOCIETY OF THORACIC SURGEONS

January 24–26, 1977
San Francisco Hilton Hotel, San Francisco, CA

January 24, 1977 (Monday)
Morning

8:00 Business Meeting (members only)

8:30–12:00 **Scientific Session**

1. Patient-Related Risk Factors as Predictors of Results following Isolated Mitral Valve Replacement
Neal W. Salomon, M.D., Edward B. Stinson, M.D., Randall B. Griepp, M.D., and Norman E. Shumway, M.D., Stanford, CA

2. Reversal of Advanced Left Ventricular Dysfunction following Aortic Valve Replacement for Aortic Stenosis
Roque Pifarré, M.D., Robert Croke, M.D., Henry Sullivan, M.D., Rolf Gunnar, M.D., and Henry Loeb, M.D., Hines, IL

3. Bacteremia, Endocarditis, and the Hancock Valve
Donald J. Magilligan, Jr., M.D., Edward L. Quinn, M.D., and Julio C. Davila, M.D., Detroit, MI

4. Late Evaluation of Patients Undergoing Valve Replacement with the Björk-Shiley Prosthesis
Derward Lepley, Jr., M.D., Harjeet M. Singh, M.D., Alejandro Aris, M.D., Robert J. Flemma, M.D., and Donald C. Mullen, M.D., Milwaukee, WI

5. Transbronchial Lung Biopsy in Diffuse Pulmonary Disease
Claude W. Smith, M.D., Gordon F. Murray, M.D., Peter J. K. Starek, M.D., David D. Delaney, M.D., and Benson R. Wilcox, M.D., Chapel Hill, NC

6. A Rational Approach to Total Thymectomy in the Treatment of Myasthenia Gravis
Alfred Jaretzki III, M.D., Morrison Bethea, M.D., Marianne Wolff, M.D., Robert E. Lovelace, M.D., Audrey S. Penn, M.D., and Louis Rowland, M.D., New York, NY

7. Gross and Microscopical Blood Supply of the Trachea
John R. Salassa, M.D., Bruce W. Pearson, M.D., and W. Spencer Payne, M.D., Rochester, MN

8. Trachea–Innominate Artery Fistula: Successful Management of 3 Consecutive Patients
Joel D. Cooper, M.D., Toronto, Ont, Canada

Afternoon

1:30–5:00 **Scientific Session**

9. Local Nerve Block Anesthesia for Peroral Endoscopy
Tom R. DeMeester, M.D., David B. Skinner, M.D., Richard H. Evans, M.D., and Donald W. Benson, M.D., Chicago, IL

10. Recommended Protocol for Pacemaker Follow-up: Analysis of 1,671 Implanted Pacers
Emil L. Mantini, M.D., Raymond K. Majors, M.D., James R. Kennedy, M.D., and George R. Lebo, M.D., Gainesville, FL

11. An Experimental Study of the Effectiveness of Various "Antireflux" Operations
Howard Leonardi, M.D., Myles E. Lee, M.D., M. Fathi El-Kurd, M.D., and F. Henry Ellis, Jr., M.D., Boston, MA

12. Reflux Control following Gastroplasty
R. D. Henderson, M.B., Toronto, Ont, Canada

13. Total Valvectomy: Treatment of Choice for Pulmonary Stenosis due to Congenital Valve Dysplasia
Levi Watkins, M.D., James S. Donahoo, M.D., Donald Harrington, M.D., Grover Hutchins, M.D., J. Alex Haller, M.D., and Catherine Neill, M.D., Baltimore, MD

14. Experience with Valved Conduits for Repair of Congenital Cardiac Lesions
William I. Norwood, M.D., Michael E. Freed, M.D., Albert P. Rocchini, M.D., and Aldo R. Castaneda, M.D., Boston, MA

15. Early and Late Results in Pulmonary Atresia with Intact Ventricular Septum
Anthony R. C. Dobell, M.D., and André Grignon, M.D., Montreal, Que, Canada

16. Left Ventricular Approach to Multiple Ventricular Septal Defects
Claudio Zavanella, M.D., Hikaru Matsuda, M.D., Fred Jara, M.D., and Sambamurthy Subramanian, M.D., Buffalo, NY

17. Early and Late Results of Transatrial Closure of Ventricular Septal Defect in Infancy
Joachim Rein, M.D., William I. Norwood, M.D., and Aldo R. Castaneda, M.D., Boston, MA

Evening
8:30–10:00 Surgical Motion Pictures

Anomalous Origin of Left Coronary Artery
Donald B. Doty, M.D., Iowa City, IA

Endoscopy under Local Anesthesia in a Sitting Position
Clement A. Hiebert, M.D., Portland, ME

Surgical Repair of Ventricular Septal Rupture Complicating Inferior Myocardial Infarction
Willard M. Daggett, M.D., Boston, MA

Coronary Artery Grafting: Two-Surgeon Interrupted Suture Technique
Richard K. Hughes, M.D., George G. Lindesmith, M.D., Quentin R. Stiles, M.D., Bernard L. Tucker, M.D., Richard J. Hurvitz, M.D., and Bertrand W. Meyer, M.D., Los Angeles, CA

Atrial Myxoma
Javier Fernandez, M.D., Browns Mills, NJ

Left Coronary Artery–Left Ventricular Fistula
Allen I. Midell, M.D., Chicago, IL

Creation of Double-Outlet Left Ventricle with Special Composite Prostheses for Left Ventricular Outflow Tract Obstruction: Results in 11 Patients
John C. Norman, M.D., Houston, TX

January 25, 1977
Morning
8:30–11:30 Scientific Session

18. Problems in Cost-Benefit Analysis for Cardiac Surgery: 1. The Variation in Hospital Charges
Alan T. Marty, M.D., Adel F. Matar, M.D., Ross Danielson, M.D., and Richard R. O'Reilly, M.D., Portland, OR

19. Assessment of Operation in the Control of Lung Cancer
Clifton F. Mountain, M.D., Houston, TX

20. Pulmonary Coccidioidomycosis: Analysis of Surgical Results
Neil George Steinhoff, M.D., and Austin Ronthwaite Grant, M.D., Phoenix, AZ

21. Bronchobiliary and Bronchopleural Fistulas
David Preston Boyd, M.D., Boston, MA

22. Surgical Resection of Multiple Pulmonary Metastases
Hiroshi Takita, M.D., Mukund S. Didolkar, M.D., Claude Merrin, M.D., and Harold O. Douglas, Jr., M.D., Buffalo, NY

23. Pulmonary Alveolar Proteinosis: Treatment with Whole-Lung Lavage in 14 Patients
Paul A. Selecky, M.D., Karlman A. Wasserman, M.D., John R. Benfield, M.D., and Maurice Lippmann, M.D., Torrance, CA

11:30–12:00 **Presidential Address**
Thomas B. Ferguson, M.D.

Afternoon
1:30–3:00 **Forum**

24. Intraoperative Doppler Coronary Artery Finder
Peter V. Moulder, M.D., Michael Teague, M.D., Victor Manuele, M.D., Richard Brunswick, M.D., and George R. Daicoff, M.D., Gainesville, FL

25. Is a Left Vent Necessary during Cardiopulmonary Bypass?
Kit V. Arom, M.D., Joseph F. Vinas, M.D., John G. Fewel, M.D., Vernon S. Bishop, M.D., Frederick L. Grover, M.D., and J. Kent Trinkle, M.D., San Antonio, TX

26. Evaluation in Vivo of an Electrically Driven Intrathoracic Left Ventricular Assist Device
Randall B. Griepp, M.D., Peer M. Portner, M.D., Allen K. Ream, M.D., Neal W. Salomon, M.D., and Steven D. Corbin, M.D., Stanford, CA

27. Canine Lung Allotransplantation: Donor Pretreatment
Melvyn Goldberg, M.D., Shing Chark Luk, M.D., David Greyson, M.D., and Alison Greenaway, M.D., Toronto, Ont, Canada

28. Gastroesophageal Reflux and Ascorbic Acid Insufficiency
Clement A. Hiebert, M.D., Portland, ME

29. Extraanatomical Bypass of the Aortic Root: An Experimental Technique for Treatment of Aortic Prosthetic Endocarditis
John W. Brown, M.D., Claudio A. Salles, M.D., and Marvin M. Kirsh, M.D., Ann Arbor, MI

30. Clinical, Roentgenological, and Hemodynamic Aspects of Experimental Cardiomyopathy
Sheldon Burman, M.D., Thomas Casale, M.D., Onkar Narula, M.D., Stephen Greenberg, Ph.D., Edward Millhouse, Ph.D., James Kamaryt, B.A., and William Schumer, M.D., North Chicago, IL

31. Advantages of Hypothermia and Potassium Cardioplegia in Left Ventricular Hypertrophy
Robert Ellis, M.D., and Paul A. Ebert, M.D., San Francisco, CA

32. Does Local Cardiac Hypothermia during Cardiopulmonary Bypass Protect the Myocardium from Long-term Morphological and Functional Injury?
Wolfgang Schraut, M.D., John J. Lamberti, M.D., Kenneth Kampman, B.S., Constantine Anagnostopoulos, M.D., and Seymour Glagov, M.D., Chicago, IL

33. Pharmacological Preservation of the Ischemic Heart
Richard E. Clark, M.D., T. Bruce Ferguson, M.D., Rafael C. Shuchleib, M.D., and Philip D. Henry, M.D., St Louis, MO

3:45–5:00 Business Session (members only)

Evening

7:00 President's Reception and Dinner

January 26, 1977 (Wednesday)
Morning
8:30–12:30 **Scientific Session**

34. Continuous Hypothermic Arrest versus Intermittent Ischemia for Myocardial Protection during Coronary Revascularization
J. Kenneth Koster, Jr., M.D., Lawrence H. Cohn, M.D., John J. Collins, Jr., M.D., James Muller, M.D., and Eliot Young, M.D., Boston, MA

35. Distal Endarterectomy: Its Role in Coronary Bypass Surgery
Wilbert J. Keon, M.D., Gerald M. FitzGibbon, M.D., Pierre Bédard, M.D., and Maurice Brais, M.D., Ottawa, Ont, Canada

36. Diagnosis of Perioperative Myocardial Infarction after Coronary Artery Bypass Surgery
    Charles H. Moore, M.D., Fallon T. Gordon, M.D., James A. Allums, M.D., T. Joseph Reeves, M.D., Thomas A. Lombardo, M.D., George W. Barclay, M.D., Alfred B. Brady, M.D., and R. Leldon Sweet, M.D., Beaumont, TX

37. Successful Course after Periarterial Myomectomy for Myocardial Bridging and Milking Effect of the Left Anterior Descending Coronary Artery
    Jacques Noble, M.D., Pierre Grondin, M.D., and Martial G. Bourassa, M.D., Montreal, Que, Canada

38. Management of Sudden Coronary Death
    Lawrence I. Bonchek, M.D., Gordon N. Olinger, M.D., Michael H. Keelan, Jr., M.D., Donald D. Tresch, M.D., and Ronald Siegel, M.D., Milwaukee, WI

39. Results and Complications of Intraaortic Balloon Counterpulsation
    Charles B. Beckman, M.D., Alexander S. Geha, M.D., Graeme L. Hammond, M.D., and Arthur E. Baue, M.D., New Haven, CT

40. Improved Myocardial Protection with Pulsation during Cardiopulmonary Bypass
    David Bregman, M.D., Michael Bailin, M.D., Frederick O. Bowman, Jr., M.D., Eduardo N. Parodi, M.D., Susan M. Haubert, M.D., Richard N. Edie, M.D., Henry M. Spotnitz, M.D., Keith Reemtsma, M.D., and James R. Malm, M.D., New York, NY

41. Coronary Flow Distribution and Dynamics during Continuous and Pulsatile Extracorporeal Circulation in Swine
    William Y. Moores, M.D., John P. Hannon, M.D., Jerry Crum, M.D., David Wilford, M.D., William Rodkey, M.D., and Jay Geasling, M.D., San Francisco, CA

42. Replacement of the Ascending Aorta and Aortic Valve with a Composite Graft: Results in 18 Patients
    Nicholas T. Kouchoukos, M.D., Robert B. Karp, M.D., and William A. Lell, M.D., Birmingham, AL

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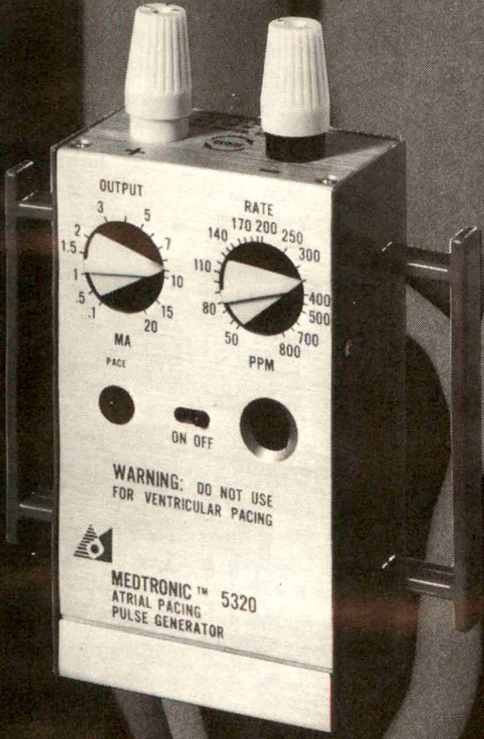

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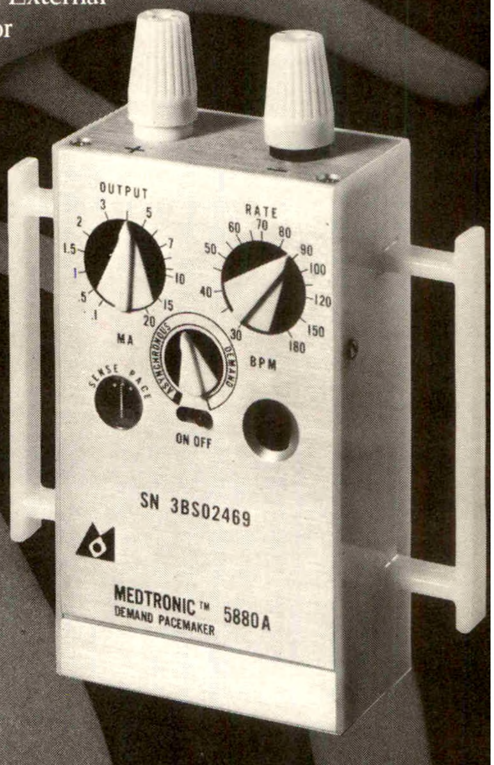

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Please respond to W-13, The Annals of Thoracic Surgery, C-7173 University Hospital, Ann Arbor, MI 48109.

Thoracic and cardiovascular surgeon, 34, married, two children, completing university residency in July, 1977, seeks position with group or association leading to partnership. Will consider all geographic locations.

Please respond to Kenneth N. Holwitt, M.D., Division of Cardiothoracic Surgery, University of Kentucky Medical Center, 800 Rose St, Lexington, KY 40504; tel (606) 278-9651.

Board-certified **thoracic surgeon,** 37, seeks position in group or association leading to partnership. Available any time, no geographic preference.

Please respond to F. B. Escano, Jr., M.D., Margaretville, NY 12455; tel (914) 586-4562.

Thoracic and cardiovascular surgeon seeks position in cardiac surgery in major academic center or in private practice with academic appointment. Experience in research and clinical aspects of thoracic and cardiac surgery. Presently staff member at prestigious academic center.

Please respond to W-16, The Annals of Thoracic Surgery, C-7173 University Hospital, Ann Arbor, MI 48109.

Thoracic and cardiovascular surgeon, 35, well trained in all aspects of thoracic and cardiovascular surgery, experience in research, seeks partnership practice in thoracic-cardiovascular surgery. FLEX, ABS certified, candidate for 1977 ABTS exam. Presently fellow in congenital cardiac surgery, Children's Hospital, Denver.

Please respond to W-17, The Annals of Thoracic Surgery, C-7173 University Hospital, Ann Arbor, MI 48109.

Thoracic and cardiovascular surgeon, 35, Board-certified, completing military obligation in August, 1977, desires position in private practice with opportunity for academic association.

Please respond to W-18, The Annals of Thoracic Surgery, C-7173 University Hospital, Ann Arbor, MI 48109.

Cardiac surgeon, trained at Groote Schuur Hospital, Cape Town, and National Heart Hospital, London, seeks academic appointment in major urban center in United States. Presently in staff position in major overseas cardiac surgery center.

Please respond to W-19, The Annals of Thoracic Surgery, C-7173 University Hospital, Ann Arbor, MI 48109.

University trained **surgeon,** 35, research experience, seeks position in cardiothoracic and vascular surgery upon completion of training, June 30, 1977. Prefer academic appointment or private group with strong academic commitment, located in Northeast. Military obligation completed.

Please respond to W-20, The Annals of Thoracic Surgery, C-7173 University Hospital, Ann Arbor, MI 48109.

Thoracic and cardiovascular surgery resident finishing in July, 1977, seeks association/partnership with active cardiothoracic surgery group. Prefer cardiac surgery. No area preference. Curriculum vitae upon request.

Please respond to Daniel A. Tatpati, M.D., 315 Palmer Dr, Fayetteville, NY 13066; tel: (315) 637-3732 after 8 PM.

Cardiothoracic surgeon, 34, married, trained at renowned New York City university medical center, seeks position in group or association leading to partnership or academic appointment. Presently staff member. Available July, 1977, no geographic preference, curriculum vitae upon request.

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Cardiovascular and thoracic surgeon, 32, completing residency in June, 1977, seeks position in group or association leading to partnership.

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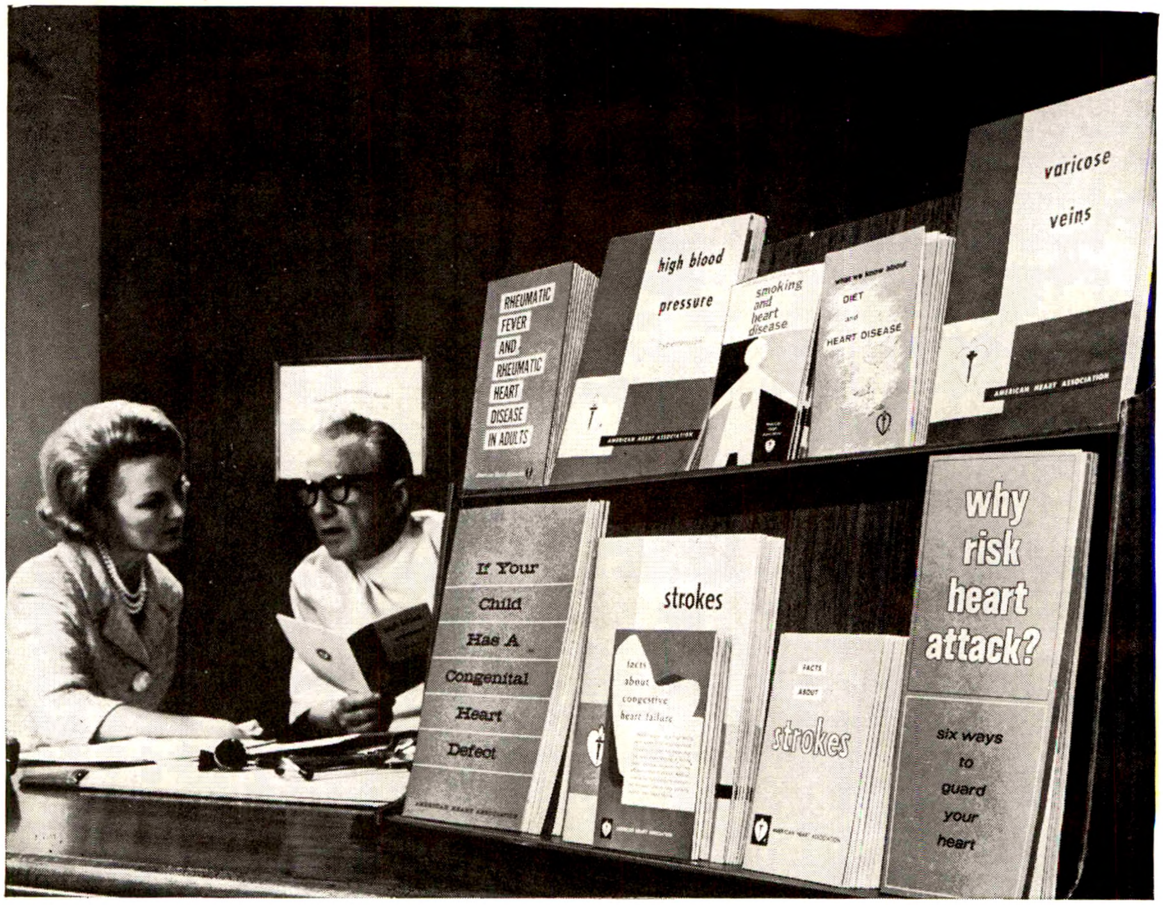
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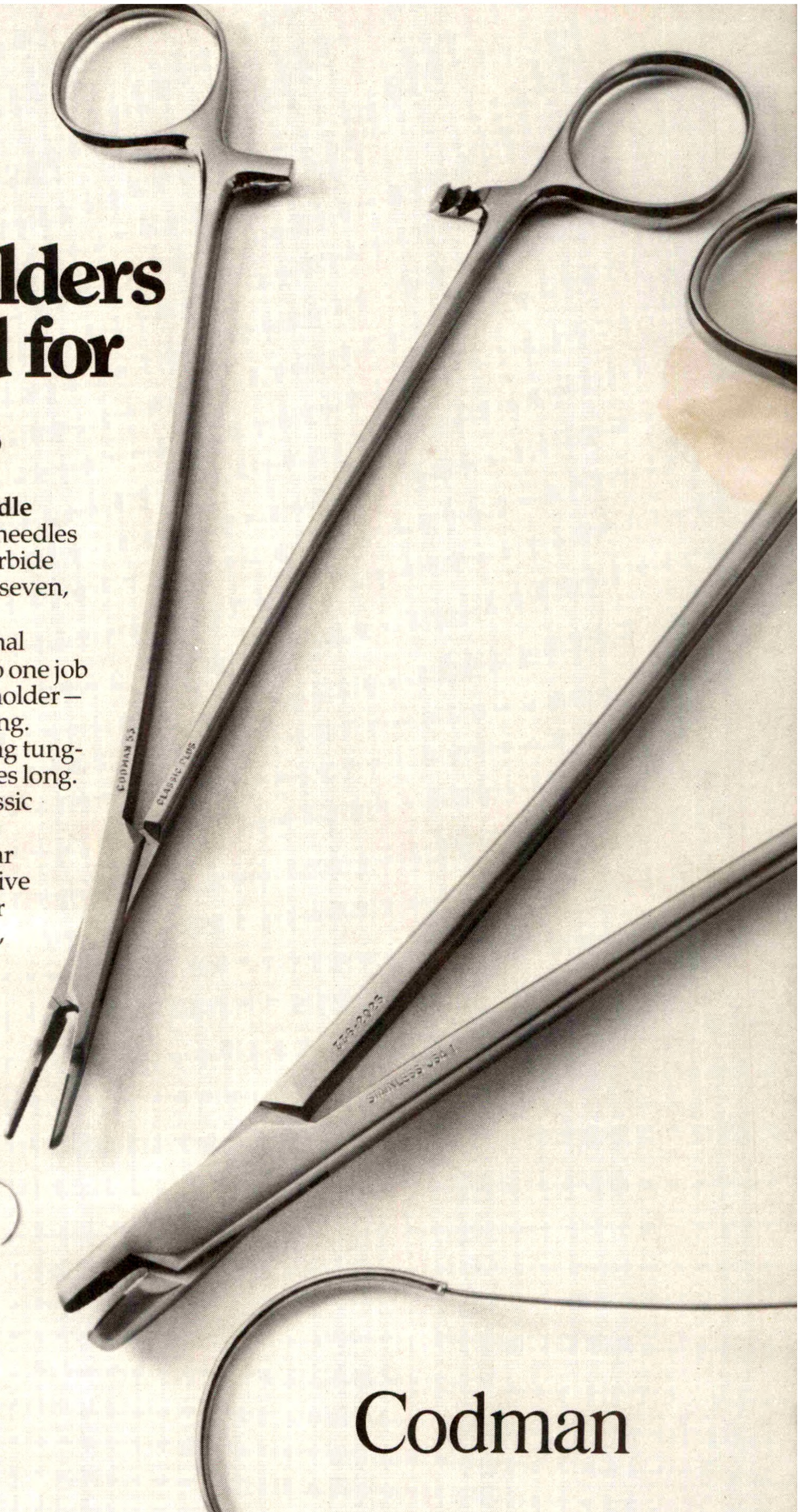

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